Investigation of extent of Interaction of Thiobarbituric acid and two selected Amino acids with Three Divalent Metal ions in Aqueous-organic medium at different Temperatures

Abstract

The formation constants of binary and ternary complexes of Thiobarbituric acid as primary ligand and L-tyrosine and L-histidine as secondary ligands have been examined in 40% (v/v) ethanol-water mixture at 27^{o}C and 35^{o}C and at ionic strength of 0.02$NaNO_3$ by potentiometric method. The ligands formed 1:1 binary complex with the metal ions. The primary and secondary ligands simultaneously coordinated to the metal ions to form 1:1:1ternary complexes. The difference in stability constants of binary and ternary complexes were detemined by ΔlogK and RS%. Ternary complexes exhibited enhanced stability than the binary complexes. The stability of the complexes decreased with increase in temperature. The thermodynamic parameters such as Gibb's free energy change (ΔG), entropy change (ΔS) and enthalpy change (ΔH) accompany the interactions were evaluated. The interactions were found to be spontaneous, exothermic, and entropically favoured.

Keyword: Stability constants,Ternary complexes,binary complexes,Thermodynamic parameters

Introduction

The study of coordination compounds in solution has provided prospects for using ligands and metal complexes in medicine, agriculture and industries(1-4). The study of complexes containing mixed ligands of amino acids and heteraromatic nitrogen base ligands with metal ions has been considered as a model for interaction between bioligands and metal ions occurring in the body system[5,6]. The knowledge of binding properties of ligands with metal ions in solution has been used as tool by chemists for quantitative and qualitative analysis of metals. Some first row transition metals are such as Co, Cu, Fe, Mn,V, and Zn are essential in sufficient quantity for normal functioning of body system due to their existence in proteins and excess of them could result to metal poisioning while some metals like Pb, As, Hg and Cd are toxic when presence in body system[7]. Chelating agents have been applied as therapeutic chelators in transportation of metal to target sites, detoxification and demetallization but most of them exhibit slow kinetic of release and toxic which may also contribute to problem of contamination[8]. As a result of these problems, researchers have been studying chelation properties of bioligands with different metal ions under different experimental conditions with a view to finding chelators that are harmless and exhibiting ease of release. Literature survey reveals paucity of work on interaction mixed-ligand of amino acids(L-tyrosine and L-histidine) and thiobarbituric acid with metal ions in aqueous-organic medium at different temperatures. This work therefore reports interactions of mixed-ligand of L-tyrosine, L-histidine and thiobarbituric acid with metal ions in ethanol-water medium with a view to providing data on their binding properties in forming binary and ternary complexes for various biological applications.

Experimental

Materials

All the chemicals used in present study were of analytical grade and were used without further purification.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-tyrosine,L-histidine and Thiobarbituric. Metal ion solutions (0.002 moldm^{-3}) and ligand solutions (0.002 moldm^{-3}) were prepared from metal nitrate and the ligands in double distilled water. The concentrations of metal solutions were standardized by titrating against EDTA solution. The stock solutions of 0.01 mol dm^{-3} HNO_3 was prepared by measuring and dissolving amounts of the acid in appropriate volume CO_2-free double distilled water. The concentration of the acid was standardized by titrating against NaOH solution. Solution of 0.134 moldm^{-3} of CO_2-free NaOH solution was prepared and standardized with oxalic acid solution. The ionic strength of each solution was adjusted to 0.02 mol dm^{-3} by addition of $NaNO_3$

Apparatus

Potentiometric titrations were carried out with Mettler Toledo(FP20 Standard) meter with accuracy ±0.03 units using combined electrode assembly. The pH meter was calibrated against standard buffers solutions (pH 4.00, 6.86 and 9.18). All the titrations were carried out within the slope of 99-105%.The temperature was maintained constant at 27 ^{o}C(± 0.1) and 35^{o}C(± 0.1) throughout the titrations. All the titrations were carried out in multiples. The pH measurements are corrected according to Van Uitert and Hass procedure[9].

Method

For determination of proton-ligand stability constants and stability constants of binary and ternary complexes in 40 % (v/v) ethanol-water, the following sets of solution were prepared and the volume was made up to 40ml and titrated against CO_2-free NaOH solution.

(1) Free HNO_3(A)
(2) Free HNO_3 + Ligand Thiobarbituric acid
(3) Free HNO_3+ Ligand Thiobarbituric acid + Metal ion
(4) Free HNO_3 + Ligands (Ltyrosine or L-histidine)
(5) Free HNO_3 + Ligands (Ltyrosine or L-histidine) + Metal Ion
(6) Free HNO_3 + Ligand Thiobarbituric acid + Ligands (Ltyrosine or L-histidine) + Metal Ion

The obtained values of pH were plotted against volume of alkali added for above sets of titration and titration curves were obtained using origin 8 program. From the curves, the equilibria existing in solution were examined by comparing the curves. The protonation constants and the formation constants of binary complexes were determined using Point wise method by calculating the average number of metal ions associated with the ligand $\overline{nA}$ at different pH values, average number of ligand molecules attached per metal ion (ñ) and free ligand exponent (pL) and formation constants of ternary complexes were determined by using Ramamoorthy and Santapa method[10]. Distributions of species were obtained by Hyperquard Simulation and Speciation program. Thermodynamic parameters such as Gibb'sfree energy change (ΔG), entropy change (ΔS) and enthalpy change (ΔH) for deprotonation of the ligands and formation of complexes were determined.

RESULTS AND DISCUSSION

Nature of potentiometric curves

The curves for the binary complexes and ternary complexes of L-tyrosine,L-histidine and Thiobarbituric acid in 40%ethanol-water at 27^{o}C are presented figure 1 for the purpose of brevity.

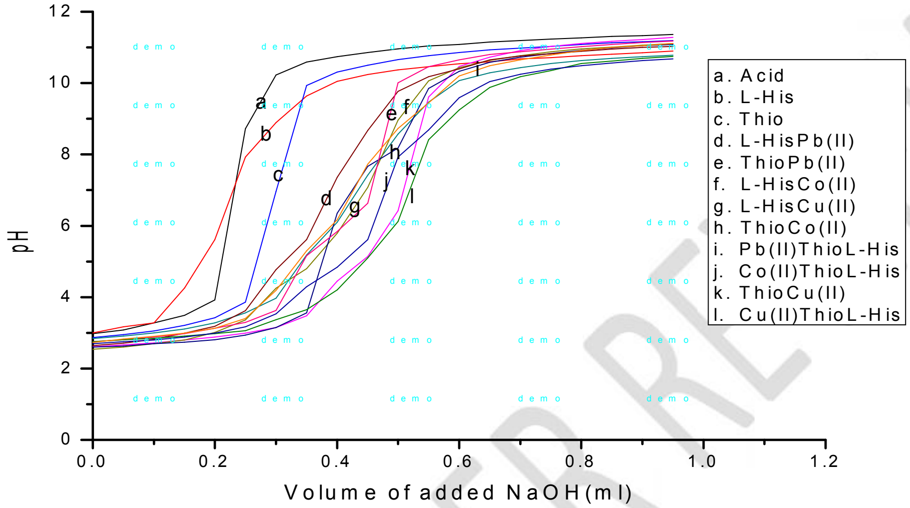

Figure 1. Potentiometric titration curves of Thiobarbituric acid(A) and L-Histidine(B) and their binary and ternary complexes in 40%ethanol-water at 27^{o}C (I=0.02M $NaNO_3$)

It is observed from the figure above that b curve shifts from acid curve to higher and lower pH while c curve deviates to lower pH region. The divergences of the curves to higher pH and lower pH in relation to the acid curve for the same volume of alkali indicate deprotonation of the ligands [11]. Addition of metal ions to each of the ligand solutions results in deviations of curves, d,e,f,g,h and k from curves b&c to a lower pH value region. This observation suggests coordination of the ligand to the metal ions occurs through displacement of proton(s) from the ligands. The i, j and l curves are found to lie below metal - ligand curves of Thio ligand and this suggests the formation of the mixed-ligand complexes. It is also observed from the figure that the ternary complexes curves do not coincide with any of binary complex curve and this indicate simultaneous coordination of the two ligands to the metal ions in the complexes [12].

Proton-ligand, Metal-ligand stability constants and effect of Temperature

From curves a, b&c in figure 1, the values of $\overline{nA}$ (the average number of protons associated with the ligand) were determined by employing the relationship derived by Irving and Rossotti [12]. These $\overline{nA}$ values were used for determination of proton-ligand stability constants of the ligands by pointwise method. Formation constants of the binary complexes were determined from ligands curves and metal-ligand curves. The average number of ligand molecules coordinated to the metal ion($\bar{n}$) and free ligand concentration(pL) were evaluated and from obtained values, metal-ligand stability constants were obtained by pointwise method in ethanol-water 40% medium[12]. Proton-ligands stability constants of the ligands and stability constants of binary complexes and their thermodynamic parameters are presented in tables 1& 2 respectively.

Table 1. Proton-ligand stability constants of the ligands at 27°C and 35°C(*I*=0.02MNaNO$_3$) and thermodynamic parameters

	27°C		35°C		ΔG(KJ/mol)			
LIgand	$LogK_1^H$	$LogK_2^H$	$LogK_1^H$	$LogK_2^H$	300K	308K	ΔH(KJ/mol)	ΔS(J/molK)
L-His	4.5944	11.0651	3.3314	10.7158	-90	-83	-357	-889
L-Tyr	3.6802	11.3279	-	11.1145	-86	-66	-861	-2582
Thio	-	11.9198	-	11.4935	-685	-68	-94	-86

Table 2. Stability constants of binary complexes at 27^{o}C and 35^{o}C(I=0.002MNaNO$_3$) and thermodynamic parameters.

Complex	LogK	300K	308K	ΔG(KJ/mol)	ΔH(KJ/mol)	ΔS(J/molK)
L-HisCu(II)	$LogK_{CuHis}^{Cu}$	7.6744	6.5231	-44	-254	-702
L-His-Co(II)	$LogK_{CoHis}^{Co}$	6.5724	6.4519	-38	-27	-137
L-His-Pb(II)	$LogK_{PbHis}^{Pb}$	7.8574	6.5585	-45	-287	-807
L-TyrCu(II)	$LogK_{CuTyr}^{Cu}$	7.5232	7.4981	-43	-6	+125
L-Tyr-Co(II)	$LogK_{CoTyr}^{Co}$	6.7419	5.9816	-39	-168	-431
L-Tyr-Pb(II)	$LogK_{PbTyr}^{Pb}$	7.2704	6.7085	-42	-124	-275
ThioCu(II)	$LogK_{CuThio}^{Cu}$	9.0645	7.5790	-52	-329	-921
Thio-Co(II)	$LogK_{CoThio}^{Co}$	7.2557	6.4497	-42	-178	-455
Thio-Pb(II)	$LogK_{PbThio}^{Pb}$	8.3048	7.4314	-48	-193	-485

Table 1 shows that dissociation of two protons and one occurs in secondary ligands(L-His and L-tyr) and primary ligand(Thio) respectively at 27^{o}C while at 35^{o}C, two protons are dissociated from L-His ligand and one from both Thio and L-Tyr ligands. The mean $LogK_2^H$ value of 11.9198 at 27^{o}C and $LogK_2^H$ of 11.4935 at 35^{o} C of Thio ligand are attributed to deprotonation of protons at N$_3$H group present in the ligand [13]. The mean values of $LogK_1^H$ equals to 3.6802 and $LogK_2^H$ equals to 11.3279 of L-Tyr at 27^{o}C are attributed to deprotonation at COOH group and amine (NH$_2$) group of the ligand respectively. L-His also shows two dissociation constants at mean $LogK_1^H$ value of 4.5944 and $LogK_2^H$ value of 11.0651 of L-His at 27^{o}C which are attributed to deprotonation at COOH group and amine (NH$_2$) group of the ligand respectively [14,15]. Only on proton is observed to be deprotonated by L-Tyro at 35^{o}C with deprotonation constant of $LogK_2^H$ equals to 11.1145 which is ascribed to deprotanation of amine (NH$_2$) group of the ligand[14]. The proton-ligand stability constant values decrease with increase in temperature showing increase in acid strength with temperature. The negative values of ΔG and ΔH respectively reveal spontanoues and exothermic deprotonation processes undergo by the ligands. The negative values of ΔS obtained are attributed to binding of greater amount of solvent molecules to the deprotonated ligand than the original amount associated with undeprotonated form[16].

All the ligands formed 1:1 binary complexes and this is confirmed by the inflection points and $\bar{n}$ evaluated average number of ligand bound per metal in range of 0.1-0.5(17). From table 2, Thio and L-Tyr interact with Cu(II), Co(II) and Pb(II) at 27^{o}C and 35^{o}C with stabilities in order of t $LogK^{Cu}_{CuTyr} > LogK^{Pb}_{PbTyr} > LogK^{Co}_{CoTyr}$ and $LogK^{Cu}_{CuThio} > LogK^{Pb}_{PbThio} > LogK^{Co}_{CoThio}$. This order is assigned to polarizability and covalent-bonding effect of the metal ions. Extra stability exhibited by Cu(II) might be due to the Jahn Teller distortion due unique configuration of the metal ion(18,19]. L-His ligand interacts with the metal ions at both temperatures to give order of $LogK^{Pb}_{PbHis} > LogK^{Cu}_{CuHis} > LogK^{Co}_{CoHis}$. The order could be attributed to covalent-bonding index and polarizability of the metals. The ligands give the order of $LogK^{Cu}_{CuThio} > LogK^{Cu}_{CuHis} > LogK^{Cu}_{CuTyr}$ at 27^{o}C and 35^{o}C which could be ascribed to the nature of donor atoms of the ligands [20,21]. The order of $LogK^{Co}_{CoThio} > LogK^{Co}_{CoTyr} > LogK^{Co}_{CoHis}$ is observed and attributed to type of donor atoms involved in the coordination, polizability and basicity of the ligand [20,22] while the order of $LogK^{Co}_{CoHis} > LogK^{Co}_{CoThio} > LogK^{Co}_{CoTyr}$ at 35^{o}C is attributed to basicity of the ligands. The order of $LogK^{Pb}_{PbThio} > LogK^{Pb}_{PbHis} > LogK^{Pb}_{PbTyr}$ at 27^{o}C is attributed to basicity of ligands and involvement of S-donor atom in Thio ligand while the order of $LogK^{Pb}_{PbThio} > LogK^{Pb}_{PbTyr} > LogK^{Pb}_{PbHis}$ at 35^{o}C is assigned to coordinating atoms and polarizability of the ligands[23,24].

In all the complexes, decrease in metal-ligand stability constant (logK) was observed with increase in temperature. The negative ΔG values indicate spontaneous complexation of the ligands to the metal ions.It is reported that the divalent metal ions exist in solution as octahedrally hydrated species [16] and the values of ΔH and ΔS can be determined by considering the combined effects of (a) dissociation of water molecules and (b) metal-ligand bond formation.Negative enthalpy change (ΔH) obtained for the interaction s between the ligands and the metals implying exothermic complexation reactions and the reactions are favourable at lower temperature and the metal-ligand binding process is enthalpy driven and metal-ligand association is fairly strong [25]. Negative values of ΔS observed in all the binary complexes indicate that complexation reactions are enthropy unfavourable due to the large amount of coordinating solvent around the ligands while positive ΔS observed in L-His-Pb(II) complex implies entropy favoured association between the ligand and the metal[26].

Stability constants of ternary complexes and thermodynamic parameters

Stability constants of ternary complexes of Thiobarbituric acid as primary ligand and L-Histdine and L-Tyrosine as secondary ligands with Cu(II),Co(II) and Pb(II) ions in 40%(v/v)ethanol-water at 27°C amd 35°C are evaluated from the formation curves. The stabilities of the ternary complexes with respects to the binary complexes are quantified by ΔlogK and RS%. The stability constants and the thermodynamic parameters are presented in table 3-7.

Table 3: Stability constants of ternary complexes of L-tyrosine and Thiobarbituric acid in 40% (v/v)ethanol-water4with I = 0.02 M ($NaNO_3$) at27°C

Complex	$LogK^{M}_{MAB}$	$LogK^{M}_{MA}$	$LogK^{MA}_{MAB}$	$LogK^{M}_{MB}$	$\Delta logK$	$RS\%$
[CuThioTyr]	15.6108	9.0645	6.5463	7.5232	-0.9797	-0.2778
[CoThioTyr]	15.2378	7.2557	7.9821	6.7419	1.2402	10.0114
[PbThioTyr]	15.9948	8.3048	7.6901	7.2704	0.4196	-7.4017

Table 4: Stability constants of ternary complexes of L-tyrosine and Thiobarbituric acid in ethanol-water40-60% with I = 0.02 M ($NaNO_3$) at 35°C

Complex	$LogK^{MA}_{MAB}$	$LogK^{M}_{MAB}$	$LogK^{M}_{MA}$	$LogK^{M}_{MB}$	$\Delta logK$	$RS\%$
[CuThioTyr]	15.1953	7.5790	7.6163	7.4981	0.1183	0.4921
[CoThioTyr]	14.0300	6.4497	7.5803	5.9816	1.5987	17.4434
[PbThioTyr]	15.4782	7.4314	8.0468	6.7034	1.3434	8.2743

Table 5: Stability constants of ternary complexes of L-histidine and Thiobarbituric acid in ethanol-water40-60% with I = 0.02 M ($NaNO_3$) at 27^{o}C

Complex	$LogK^{M}_{MAB}$	$LogK^{M}_{MA}$	$LogK^{MA}_{MAB}$	$LogK^{M}_{MB}$	$\Delta logK$	$RS\%$
[CuThioHis]	17.6925	9.0645	8.6280	7.6744	0.9536	-4.8154
[CoThioHis]	15.2314	7.2557	7.9757	6.5724	0.6833	10.2247
[PbThioHis]	16.2401	8.3048	7.9353	7.8574	1.7723	-4.4492

Table 6: Stability constants of ternary complexes of L-histidine and Thiobarbituric acid in ethanol-water40-60% with I = 0.02 M ($NaNO_3$) at 35^{o}C

Complex	$LogK^{M}_{MAB}$	$LogK^{M}_{MA}$	$LogK^{MA}_{MAB}$	$LogK^{M}_{MB}$	$\Delta logK$	$RS\%$
[CuThioHis]	16.1824	7.5790	8.6034	6.5231	2.0803	13.5163
[CoThioHis]	14.8441	6.4497	8.3944	6.4519	1.9445	30.1518
[PbThioHis]	15.7759	7.4314	8.3445	6.5585	1.7860	12.2871

Table 7: Thermodynamic parameters of ternary complexes of L-histidine and Thiobarbituric acid

	ΔG(KJ/mol)	ΔG(KJ/mol)	ΔH(KJ/mol)	ΔS(J/mol)	ΔS(J/mol)
Complex	300K	308K		300K	308K
[CuThioHis]	-102	-95	-334	-774	-774
[CoThioHis]	-87	-88	-86	6	6
[PbThioHis]	-93	-93	-103	-31	-31
[CuThioTyr]	-90	-90	-92	-7	-7
[CoThioTyr]	-88	-82	-267	-599	-599
[PbThioTyr]	-92	-91	-114	-75	-75

In the tables Δlog K was found to be positive for all the complexes except Cu(II) ternary complex of L-tyrosine and Thiobarbituric acid at 27^{o}C. The positive Δlog K reveals more stability of the complexes than their corresponding binary complexes.The positive value of RS% affirmed the existence of enhanced stability. The enhanced stability could be attributed to intramolecular aromatic-ring stacking and hydrogen bond while negative Δlog K implies less stability of the ternary complexes than the binary complex of secondary ligand[27]. The stability is also attributed to increase in polarity as a result of redistribution of the electron densities of the metal-ligand bond in ternary therefore mixed ligand complexes are not easily hydrolysed[28,29]. Co(II) ternary complexes exhibited more stability than the corresponding binary complexes among the ternary complexes and this is established by the values of Δlog K and RS%. The decrease in stability values of the complexes with increase in temperature as shown in the tables indicates that complexation of the ligands is favourable at lower temperature. A negative ΔG values for all the complexes suggest spontaneous complexation reaction. Negative values of ΔH show that the chelation processes are exothermic and favorable at very low temperature[11]. In all the ternary complexes of L-histidine, the order of stability is found to be Cu(II)>Pb(II)>Co(II) . This order could be attributed to tetragonal distortion of Cu(II) geometry which gives extra stability to the metal complexes[30]. In all the ternary complexes of L-tyrosine, the stability is in order of $\mathrm{Pb(II)} > Cu(\mathrm{II}) > Co(II)$ and the extra stability exhibited by Pb(II) complexes could be attributed to increase in covalent –bonding index,polarizability of the metal ions and polarizability of ligand. At both temperatures, all the ternary complexes of L-histidine, except Co(II) ternary complex at 27^{o}C, are more stable than the ternary complexes of L-tyrosine.The more stability of the ternary complexes is attributed to coordination of the ligand through nitrogen donor atoms of imidazole and amino groups[24].

Conclusion

Interaction of L-histindine,L-tyrosine and Thiobarbituric acid with Cu(II), Co(II) and Pb(II) ions in % (v/v) ethanol–water mixture at different temperatures have been determined by potentiometric method. The metal ions formed binary (1:1) and (1:1:1) ternary complexes with the ligands. The stability of the complexes is affected by basicity of the ligand, nature of donor atoms, polarizability of ligands, covalent-bonding index and polarizability of the metal ions. The stability of the ternary complexes with respect to binary complexes was determined by ΔlogK and RS%. The positive values of ΔlogK and high values of RS% affirmed more stability of the ternary complex than the corresponding binary complex while negative value of ΔlogK established less stability of ternary complex than the binary complex. The deprotonation constants of the ligands and metal-ligand stability constants decrease with increase in temperature. Thermodynamic evaluation revealed spontaneous, exothermic and entropically favoured and unfavoured complexation process.Thiobarbituric acid and L-histidine ligands showed high affinity for Pb(II) ion while L-tyrosine exhibited high affinity for Cu(II) ion. The mixed-ligand of L-histidine and Thiobarbituric acid showed high affinity for Pb(II) ion while mixed ligand of L-tyrosine and Thiobarbituric acid showed high affinity for Cu(II) ion. The individual ligand and their mixture can be used for extraction,transportation and detoxification of metals.

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