



Formation Of Binary And Mixed Ligand Complexes Of DL- Pencillamine And Its Toxic Metals

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Abstract

The Co-ordination of chemistry in the field of medical science is appreciable in treating metal poisoning by chelation therapy with the help of chelating agents, the co-ordination compounds play an important role in the biological system and the current Chelating agents form soluble stable non-toxic complexes which can readily be excreted elements which are commonly available in nature are non-toxic at normal levels but they are harmful at higher concentrations. The elements like As, Pb, Cd, Hg etc. entered in to ecosystem with rapid progress of our civilization. The living kingdom is exposed to such uncommon elements leading to adverse effect (or) Toxic effect there are certain agents which reduces the toxic effect of chelating agent due to the stable complex form of chelating agents and it shield effects to toxic metal its may also shield the biological effects and reduced the toxicity, chelating agents may expose metal to the biological environment and prevent the metal from being scavenged by biological protective mechanism. There by toxicity may increase. Example: DDC (Diethy lldithio carbamate) which enhances brain deposition of Cd, PB, Ni, Cu, Zn, Hg etc. The DL- Pencillamine is one of the potential chelating agents which are used for detoxification. It's a drug use for treating patients suffering from Wilson's disease it also create urinary excretion of copper metal from the biological system. This article includes the formation of mixed and binary ligand complexes of DL- Pencillamine with N-O- donors and toxic metals.

Introduction

The Metal complexes have gained importance owing to their applications in different fields like analytical chemistry, industry and biological systems. It is well known that the binary and ternary complexes play an important role in biological processes in which enzymes are known to be activated by metal ions, in analytical chemistry, binary and ternary metal complexes been used in the spectrophotometric determination of the number of metal ions. IN recent years most of the investigations on the study of metal complexes both in solid and solution state have attained much importance. Because of their remarkable complexing properties. Under biological and environmental condition multiligand - multi-metal ion equilibria dominate strongly, (i.e.)

mixed-liged or higher order complexes are formed. Per definition the most simple of these species, (i.e.) a ternary complex" will consist of a metal ion and two different ligands, other than solvent. Such catalyzed reactions⁷, they appear in biological fluids, create specific structures, and manifest themselves as enzymes-metal ion substrate complex and in the detection of tumours. In living organisms ternary metal complexes take part in the functions of metalloenzymes, transport of metal ions, and transport of oxygen. It is believed that most of the enzymes require the presence of a metal ion for their catalytic activity transport of metal ions such as Fe^{+2} , Cu^{+2} etc. in living organisms also involves metal complex formations. For example most of non-protein bound Cu(II) in blood plasma is present in the form of ternary metal complexes vitamin B_{12} is the best example for mixed ligand in which cobaltous ion is bound to pyrrole nitrogen's. metal complexes have been used to treat various diseases. Binary complexes Pt(II) are known as anti-tumours agent used treatment of cancer. The coordination chemistry can be treated as a meeting place of all branches of chemistry. Thus its become understandable why mixed ligands systems have been used to treat various diseases. Binary complexes of Pt(II) are known as anti-tumour agents used in the treatment of cancer. The coordination chemistry can be treated as a meeting place of all branches of chemistry. Thus it's become understandable why mixed ligands systems have recently been receiving more and more attention. the work coordination chemistry is of fundamental importance and is a topic of current wider interest. A coordination compound contains a central metal ion surrounded by a set of molecules or ions known as ligands and capable of existing independently. a ligand is a molecule or ion that can donate an electron pair to the central metal cation. Some of these donors occur in a set of two are more on a complex ligand simultaneously with the same ion resulting in a structure said to be the chelating compound. Such ligand are called chelating ligands.

Dissociation constants of Ligands (L and A)

$t=27^{\circ}\text{C}$, 37°C , 47°C . $\mu=0.15\text{ M KNO}_3$

$t=27.0^{\circ}\text{C}$; $\mu = 0.15\text{ M KNO}_3$

Ligand L or A	pK_a	pK_{2a}	pK_{3a}
DL- Pencillamine	3.10	7.246	11.358
Glycine	4.62	9.45	-
α -Alanine	2.36	9.59	-
Phenylalanine	2.38	9.3	-
Tyrosine	2.25	9.84	-
Tryptophan	2.56	9.44	16.82
Methionine	2.21	9.10	-
Lysine	2.42	10.40	-
Histidine	2.24	6.54	-

Asparticacid	3.71	9.68	-
Leu	2.40	9.52	
Serine	2.38	8.77	-
Threonine	2.32	9.03	

***Dissociation constants of N–O donor ligands (A)**

t = 27°C μ = 0.15 M KNO₃

LIGAND	Log β_{MLA}^M	Log β_{ML}^M	Log β_{MLA}^{ML}	Log $\beta_{MLA}^{ML} - \text{Log } \beta_{MA}^M$	ΔLog K
GLY	15.77	11.66	4.11	4.11 -5.84	-1.73
ALA	15.01	11.66	3.35	3.35-4.82	-1.57
METH	13.35	11.66	1.69	1.69-2.87	-1.18
LEU	13.37	11.66	1.71	1.71-3.14	-1.43
SERINE	14.24	11.66	2.64	2.64 -3.78	-1.14
THREONINE	13.80	11.66	2.14	2.14 -3.89	-1.75
LYS	14.58	11.66	2.92	2.92-3.85	-0.93
PHY ALA	13.89	11.66	2.23	2.23-3.26	-1.03
TYRO	16.38	11.66	4.29	4.29-4.27	-0.46
TRYP	12.52	11.66	0.86	0.86-3.77	-2.91
HIS	15.24	11.66	3.58	3.58-4.72	-1.14
ASP	14.76	11.66	3.10	3.10-5.04	-1.94

Formation constant for Binary cd (II) complexes with N-O**Donar Ligands (A)****T=27°C μ =0.15M (KNO₃)**

Ligand A	Log KM_{MA}
Glycine	6.0
α	5.9
Phenylalanine	7.2
Leucine	3.67
Methionine	6.4
Lysine	-
Tryptophan	7.0
Histidine	4.72
Aspartic Acid	3.61

Formation constant for Binary cd (II) complexes with N-O**Donar Ligands (A)****T=27°C μ =0.15M (KNO₃)**

Ligand and Metal	Log^MK
DL-Pencillamine+Cd	12.84
DL-Pencillamine+Ni	15.40
DL-Pencillamine+pb	14.28

Methodology

- The acid dissociation constant and stability constant for the binary and mixed ligand complexes were determined by potentiometric titrations of the ligands in the absence and presence of metal ion using standard carbonate free sodium hydroxide.
- The temperature of the system was maintained at 27, 37 and 47° C the ionic strength of the solution was maintained constant at μ =0.15M by using KNO₃ as supporting electrolyte.
- The glass electrode was used to determine the hydrogen ion concentration the pH regions below 3.5 and above 10.5 were calibrated by measurements in HCl and NaOH solutions respectively.
- The pH meter readings were noted after addition of small increments of stranded NaOH.
- The concentration of the ligand was taken 1×10^{-3} M
- In the determination of stability constant of the mono and bis binary complexes a 1:1 and 1:2 metal ligand ratio were taken and stability constant of mixed ligand complexes were determined using solutions containing a) 1:1:1 and 1:1:2 molar ration of metal ligand and secondary ligand.
- Protonation constant of free ligands mono binary complexes (ML), binary complexes (ML₂) and mixed ligand complexes MLA and MLA₂ were calculated by a sophisticated computer program BEST and SCOGS.
- Thermodynamic parameters ΔG , ΔH , ΔS were calculated.
- The thermodynamic parameters ΔH , ΔS will provide more understanding of the nature of M-L interaction both in binary and ternary systems in solutions.
- Formation constants for binary Cd, Ni and Pb can be compared by considering their formation constants.
- The % of various species formed at different PH is known by their graph for primary ligand.
 - The mixed ligand complexes have studied by doing PH titrations of metal, primary ligand and with various secondary ligands having donors.

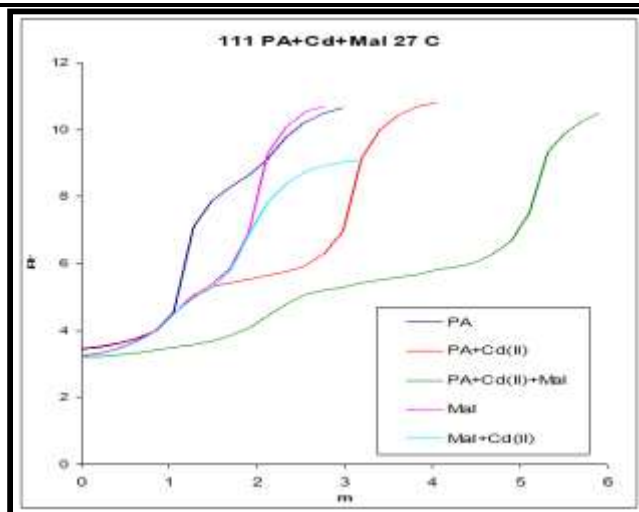


Figure 1

- The mixed ligand complexes with aliphatic donors showing one type of values and aromatic compounds showing different values.
- The aliphatic donors are less stable than aromatic compounds. In Tryp, Tyro, Phenyl Ala is more stable.
- The $\Delta \log K$ value negative values were observed for N-O⁻ donors.
- Synthesis of binary complexes of DL-Pencillamine and Cd were carried out.

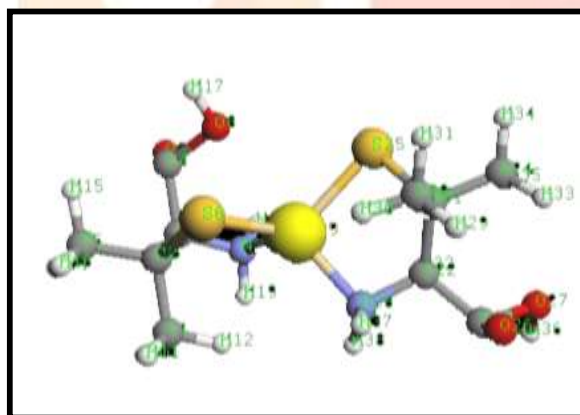


Figure 2

- The structural characterization of the synthesized Cd (II), Pb (II) and Ni (II) spectral studies binary complexes has been done using, elemental analysis, AAS, IR, UV, Mass spectra, magnetic susceptibility, TGA, DTA and molecular modeling studies.

CONCLUSIONS

The studies of mixed ligand complexes with N-O donors at temperatures 47°C when compared with aliphatic donors are less stable than aromatic compounds. In Tryp, Tyro, Phenyl Ala is more stable the complexes at 27°C are more stable than 37 & 47°C. As Temperature increases the stability of complexes decreases. The thermodynamic factors ΔH values are negative and ΔG , ΔS values were positive. In solid state the 1:2 complexes are more stable than 1:1 complexes. The geometry assigned to Cadmium complexes are tetrahedral the studies of toxicity on rat cells and antimicrobial activity were carried out using free ligand, free metal ions, binary and ternary complexes of DL-Pencillamine. The study reveals that the viability of living cells is same for all the toxic metal.

Antimicrobial activity for free ligand, free metal ions, binary and ternary complexes of DL-Pecillamine concludes that the extent of zone of inhibition around the disc indicates that the organism *Staphylococcus aureus*, *Pseudo.auriginosa* was inhibited by the compounds. The inhibition zone was more for free ligand and free metal than binary and ternary complexes. DL-Pencillamine can be used as drug for removing toxic metals like cadmium.

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