

Summary

6.1. Introduction

The coordination behavior of metal ions (essential and toxic both) play a very significant role in the area of analytical, environmental and biological chemistry.^[1-25] Metal chelation and its relationship with different biological process present a promising area of research and designing novel therapeutic methodology to deal with medical problems.^[26-33] Detoxification of metals in living organisms done by chelation therapy is an intravenous treatment designed to bind heavy metal(s) with ligand(s) in body leading to the formation of non-toxic soluble complex species. There have been now links between chelation therapy and stability of binary and ternary complexes in solution as mixed chelation occurs commonly in biological fluids i.e. a million of potential ligands are likely to form complex with metal ions found in *vivo*^[34-37]. Further many chemical processes natural and artificial both, proceed through competitive reactions involving concomitant equilibria. An immense amount of equilibrium data is available in different volumes published by Martell and Smith.^[38-42] The chemistry of metal-complex equilibria is well presented in several books, monographs and reviews.^[43-54]

The selective binding between metal(s) and ligand(s) is governed by various factors. Hence it becomes indispensable to develop indepth knowledge of interaction of metal ions with ligands that bear biological and environmental significance, under specified experimental conditions. This can be done by invoking the simple element of solution equilibria and by using computer program for calculation of equilibrium species concentration. The present piece of work includes the equilibrium studies

of hitherto unreported metal-ligand systems (binary and ternary both). The investigations are done using potentiometric technique under specified experimental conditions. Experiments are done in aqueous medium at three different temperatures and ionic strengths. Computer program SCOGS is used for obtaining the speciation profiles.

6.2. Metals and ligands selected for present work:

Owing to presence of vacant orbitals the transition and inner-transition metal ions have excellent complex forming tendencies. Further they are known to have small radii and variable coordination number which facilitates them to form complexes of varying structures and varying properties. Considerable attention is given to metal complex of transition and inner-transition metals as they find applications in various fields. Survey of literature reveals that most of the work is based on synthesis and structure analysis of these complexes. However the solution equilibrium studies need more emphasis. Hence it was decided to carry equilibrium studies involving transition and inner-transition metal ions.

The metal ions chosen are Cd(II), Gd(III), UO₂(II) and VO(II). The choice was induced by the fact that the Cd(II), Gd(III) and UO₂(II) are recognized as toxic metal ions. VO(II) ion is recognized as important catalyst exerting defense and protection functions and also a cofactor of nitrogenase in the fixation of dinitrogen. Some complexes of VO(II) have shown insulin-mimetic actions. Further these metal ions and their complexes bear significant role in biochemistry and environmental chemistry. The studies are carried with simple cations (Cd²⁺ and Gd³⁺) and oxocations (UO²⁺ and VO²⁺). This gives a comparative idea of complexation tendencies of simple cations and oxocations.

All the ternary systems investigated in the present work involve malonic acid (MAL) as one of the component. The choice of this ligand owes to its great biological significance as described in chapter-2.

The other ligands used belong to two different groups-

(1). Aminopolycarboxylic acids (NTA/IMDA)

(2). Catecholamines (TYR/DOPA/DOPM)

Where,

NTA – Nitrilotriacetic acid

IMDA – Iminodiacetic acid

TYR – Tyrosine

DOPA - 3,4-dihydroxyphenylalanine

DOPM – Dopamine

The significance of these ligands is described in chapter-2 and chapter-4 of the thesis.

6.3. Objective:

The objective of the work is to explore the multiple equilibria existing between the selected metals and ligands. Speciation profile of various complex species is obtained which can give useful information of the distribution of various species of oxocations and simple cations moieties in biological and environmental systems. Further experimental conditions are specified to correlate the effect of temperature and ionic strength on complexation equilibria. This can help in deciding the conditions for maximal formation of particular complex species.

6.4. Experimental and computational techniques:

Investigation of various binary and ternary systems is done by potentiometric method at three different ionic strengths ($\mu=0.05\text{M}$, 0.10M , 0.15M) and three different temperatures ($20\pm 1^\circ\text{C}$, $30\pm 1^\circ\text{C}$ and $40\pm 1^\circ\text{C}$) in aqueous medium.

The experimental data was subjected to rigorous mathematical treatment and computational analysis. Algebraic method of Martell and Chaberek as modified by Dey et al.^[55-57] is employed for obtaining the thermodynamic constants of various metal-ligand species. Speciation profiles are obtained by applying SCOGS (stability constants of generalized species) computer program.^[58-61] Thermodynamic parameters ΔG° (standard free energy change), ΔH° (standard enthalpy change) and ΔS° (standard entropy change) are obtained using Van't Hoff isotherm and least square fit method.^[62]

The details of the mathematical approaches and computer program used in the present work are given in chapter -1 of the thesis.

6.5. Present work:

Various binary and ternary systems investigated in the present work are presented in chapters 2-4 of the thesis.

Chapter-2 incorporates the details of the investigations and computational analysis of the following mixed ligand systems.

- 1). Cd(II) – MAL – NTA
- 2). Cd(II) – MAL – IMDA
- 3). Gd(III) – MAL – NTA
- 4). Gd(III) – MAL – IMDA

Chapter-3 comprises the results of the following mixed ligand systems.

- 1). $\text{UO}_2(\text{II}) - \text{MAL} - \text{NTA}$
- 2). $\text{UO}_2(\text{II}) - \text{MAL} - \text{IMDA}$
- 3). $\text{VO}(\text{II}) - \text{MAL} - \text{NTA}$
- 4). $\text{VO}(\text{II}) - \text{MAL} - \text{IMDA}$

Following ternary systems are included in chapter-4

- 1). $\text{Cd}(\text{II}) - \text{MAL} - \text{TYR}$
- 2). $\text{Cd}(\text{II}) - \text{MAL} - \text{DOPA}$
- 3). $\text{Cd}(\text{II}) - \text{MAL} - \text{DOPM}$
- 4). $\text{Gd}(\text{III}) - \text{MAL} - \text{TYR}$
- 5). $\text{Gd}(\text{III}) - \text{MAL} - \text{DOPA}$
- 6). $\text{Gd}(\text{III}) - \text{MAL} - \text{DOPM}$

The results of the following mixed ligand systems are presented in chapter - 5.

- 1). $\text{UO}_2(\text{II}) - \text{MAL} - \text{TYR}$
- 2). $\text{UO}_2(\text{II}) - \text{MAL} - \text{DOPA}$
- 3). $\text{UO}_2(\text{II}) - \text{MAL} - \text{DOPM}$
- 4). $\text{UO}_2(\text{II}) - \text{MAL} - \text{TYR}$
- 5). $\text{UO}_2(\text{II}) - \text{MAL} - \text{DOPA}$
- 6). $\text{UO}_2(\text{II}) - \text{MAL} - \text{DOPM}$

Apart from these ternary systems, the binary systems involving all the selected metals and ligands are investigated under the identical experimental conditions and are included in the respective chapters in order to have a comparative account of binary and ternary systems.

6.6. Results:

Potentiometric data is used to obtain titration curves (plot of pH vs 'a' where 'a' is the moles of alkali added per moles of metal / ligand). These curves were analysed to predict the formation of various species. The computation of the data is done in order to obtain speciation profiles in the form of distribution curves which demonstrate the existence of different species formed in a particular equilibrium.

The analysis of titration curves and species distribution diagrams reveals that complexes are formed by either of the following modes-

- 1). Simultaneous coordination of two ligands
- 2). Stepwise coordination of two ligands

The simultaneous mode of coordination is observed in ternary systems involving aminopolycarboxylic acids (NTA/IMDA) and malonic acid. The observation is same with all the metal cations /oxocations. This can be explained on the basis of the fact that the two ligands i.e. malonic acid (Ligand A) and aminopolycarboxylic acid NTA /IMDA (Ligand B) have no much of basicity difference as predicted from the proton dissociation constants of these ligands. (Ref. table 2.1, chapter-2). Hence the two ligands coordinate simultaneously to the metal ion in the equilibrium reaction. The thermodynamic stabilities of binary and ternary complexes of NTA (potentially tetradentate ligand) is found to be greater than IMDA (potentially tridentate ligand). This is in accordance to be expected trend.

Formation of mixed ligand complexes through stepwise equilibria is observed in case of ternary systems involving catecholamines (TYR/DOPA/DOPM) and malonic acid. Again the coordination mode is same with all the metal ions under investigations. Hence it becomes obvious that the complexation equilibria are governed more by the nature of ligands as compared to metals.

In case of metal-malonic-catecholamine ternary systems, ligand A i.e. malonic acid dissociates at lower pH whereas catecholamines tyr/ dopa/ dopm acting as ligand B undergo proton dissociation at very high pH (Ref. table 4.1, chapter-4). This indicates that the basicity of ligand B is much more than ligand A. This basicity difference leads to the formation of MA complex primarily, hence ligand A is defined as primary ligand. Ligand B acts as secondary ligand and coordinates with MA complex leading to the formation of mixed ligand species.

Comparing the stabilities of ternary complexes involving tyr/dopa/dopm, it is observed that most stable ternary complexes are formed with dopm. This is in agreement with the fact that dopm is most basic amongst the selected ligands. The binding of dopm to the metal may be assumed to be via the amino group and by bridging any one of the phenolato oxygen. In such mode it forms eight membered chelate ring which is considered to be sterically unfavorable due to large size. Alternatively, metal can bind to dopm with two phenolato oxygen and form five membered ring. This type of binding is favorable as reported earlier.^[63] Hence it is understood that dopm binds to the metal ion in pyrocatechol mode.

Comparing the stability of metal-ligand species (binary and ternary) of dopm and dopa it is seen that more stable complex are formed in the former case. This is due to less steric hindrance and small size of dopm as

compared to dopa. Dopa coordinates with metal ion in glycine like mode in lower pH range. This is in confirmation with the earlier reports which state that dopa behaves as ambidentate ligand changing its coordination mode depending on pH.^[64-68] It is established that at higher pH dopa coordinates in pyrocatechol mode consequently leading to polymeric species.^[69] Thus, computation of formation constants at higher pH is erroneous. Hence, calculations are confined below $\text{pH} \approx 8.0$.

Tyrosine bears structural similarity to dopa, hence the stability constant values with these ligands are nearly same. This indicates that both the ligands coordinate with the metal in glycine like mode. However, the slightly lower values of equilibrium constants obtained in case of tyrosine as compared to dopa can be attributed due to their basicity difference and presence of additional hydroxyl group in dopa.

Comparing the thermodynamic stability constants for various binary and ternary complex species of Cd(II) and Gd(III) it is observed that Gd(III) complex species are more stable than Cd(II).

This can be explained on the basis of high charge and higher coordination number of Gd(III) ion.

The VO(II) complexes are more stable than UO₂(II) complexes. The difference in thermodynamic stabilities under identical conditions in case of oxovanadium(IV) and dioxouranium(VI) were corroborated with the ligand preorganization and metal ion steric effects. The presence of one and two axial oxygen atoms in case of oxovanadium(IV) and dioxouranium(VI), respectively, creates less steric restriction in case of oxovanadium(IV) than dioxouranium(VI).^[8-70]

The relative stability of binary and ternary species is obtained in the form of $\Delta \log K$. $\Delta \log K$ for complexes involving simultaneous equilibria are obtained by following relation.

$$\Delta \log K_{MAB} = \log \beta_{MAB} - (\log \beta_{MA} + \log \beta_{MB}) \quad \text{----(1)}$$

The value of $\Delta \log K$ in case of aminopolycarboxylic acids with all the metal ions is found to be positive. The positive value of $\Delta \log K$ indicates that the ternary complexes are more stable than their binary analogues.

The systems where stepwise equilibria exist, $\Delta \log K$ is obtained through following relation-

$$\Delta \log K_{MAB} = \log K_{MAB}^{MA} - \log K_{MB}^M \quad \text{----(2)}$$

The reaction represents the following overall equilibrium:

$$\Delta \log K_{MAB} = \log \beta_{MAB} - \log \beta_{MA} - \log \beta_{MB} \quad \text{----(3)}$$

In most of the systems values of $\Delta \log K$ are found to be positive which indicate that the ternary complexes are more stable than the binary complexes. This is perhaps due to the complete satisfaction of primary valency (oxidation number) and the secondary valency (coordination number) of metal cations, thereby leading to more stable complexes. The negative value in some ternary systems of Cd(II) can be attributed to the availability of less number of coordination sites on binary complexes of Cd(II) thereby decreasing the flexibility of secondary ligand B to coordinate with MA species. Further MA complex of Gd(III) bears mono-negative charge whereas that of Cd(II) bears di-negative charge. Hence the secondary ligand B has to face greater repulsion in the latter case, which in turn leads to negative value of $\Delta \log K$. In $UO_2(II)$ systems the negative values of $\Delta \log K$ can be attributed to the steric hindrance due to the presence of two axial oxygen atoms.

The values of the thermodynamic stability constant $K^{\mu \rightarrow 0}$ are used to determine the ligational standard free energy change (ΔG°) for the complexation reaction from Van't Hoff isotherm:

$$\Delta G^\circ = -2.303RT \log K^{\mu \rightarrow 0} \quad \text{----- (4)}$$

The Gibb's Helmholtz equation is:

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \quad \text{----- (5)}$$

This can be written as equation (6) by putting $\Delta G^\circ = -2.303RT \log K^{\mu \rightarrow 0}$

$$\log K^{\mu \rightarrow 0} = \frac{-\Delta H^\circ}{2.303R} \frac{1}{T} + \frac{\Delta S^\circ}{2.303R} \quad \text{----- (6)}$$

The standard enthalpy change (ΔH°) and entropy change (ΔS°) have been determined by linear least square fit method by plotting a graph between $\frac{1}{T}$ vs $\log K^{\mu \rightarrow 0}$. In equation (6)-

$$\text{Slope} = \frac{-\Delta H^\circ}{2.303R} \quad \text{and} \quad \text{Intercept} = \frac{\Delta S^\circ}{2.303R}$$

Thermodynamic parameters such as ΔG° , ΔH° and ΔS° are calculated. It is found that the values of ΔG° and ΔH° are negative for all the systems which show that the complexation reaction is spontaneous and exothermic. This is further supported by positive ΔS° change in most of the cases. However, negative (ΔS°) values in some of the systems indicate a highly solvated metal complexes.

6.7. References:

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