

Computer Simulated Distribution of Co(II) in Protonated and Nonprotonated Biligand species involving Some Neurotransmitters

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ABSTRACT: Dopamine is a well known neurotransmitter and competes with other ligands in biofluids forming various protonated and nonprotonated complexes. Present paper deals with the distribution of Co(II) in MABH₃, MABH₂, MABH and MAB type triprotonated, diprotonated, monoprotated and non-protonated biligand complexes with dopamine (DOPM) (ligand A) and L-alanine, L-phenylalanine, L-aspartic acid and L-glutamic acid (ligand B). ΔG° , ΔH° and ΔS° of formation of these complexes were also determined. Percentage distribution for all the possible binary and ternary complexes was obtained by using SCOGS computer program. Coordination behaviour of ligands and possible protonation sites in the protonated complexes formed in these systems are discussed.

KEYWORDS: protonated and non-protonated complexes, ternary complexes.

I. INTRODUCTION

Dopamine belongs to the class of neurotransmitters and plays key role in signal transduction[1]. Shortage of dopamine causes Parkinson's disease[2]. Stability behaviour of complexes of dopamine with some transition, inner transition and toxic metal ions has been well documented. Present communication describes formation of various protonated and nonprotonated complexes in Co(II)-DOPM-Ala/Phe/Asp/Glu (1:1:1) mixed coordinated systems (where, DOPM = dopamine, Ala = L-alanine, Phe = L-phenylalanine, Asp = L-aspartic acid and Glu = L-glutamic acid). All the other ligands undertaken in this piece of work are building blocks of proteins and are also known to contribute to CNS[3,4].

Cobalt is central component of vitamin cobalamine or vitamin B12 and is involved in many biological complexation reactions[5]. It is essential for human in small amounts.

II. RELATED WORK

Involvement of metal complexes in plant and animal physiology has promoted *in-vitro* investigations on the systems of biological relevance[6-14]. Literature survey reveals much attention has been focused on catechols and catecholamines and other neurotransmitters as chelating agent during past few decades[7-14]. M.S. Nair *et.al.* have studied equilibrium of complexes of essential metal ions with dopa, dopamine and dimer of amino acids[10,11,25]. R. Nair *et.al.* have reported results on 4-methyl catechol, and catecholamine[7,8]. Equilibrium and spectroscopic studies on dopa were carried out by P.K. Bhattacharya *et.al.*[12].

To understand role of metal ions in Central Nervous System (CNS), we carried out studies on mixed coordinated systems involving dopa, dopamine and some biologically active ligands with toxic and nutrient metal ions[15-17]. In the same sequence, we report distribution and thermodynamic parameters of Co(II) with dopamine and some neurotransmitters.

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III. EXPERIMENTAL

All the reagents used were highest purity Merck/Aldrich products. Solutions were prepared in CO₂-free deionized water. pH-measurements were made by using Elico digital pH-meter model LI-127 with ATC probe and combined electrode type (CL-51B- Glass Body; range 0-14 pH unit; 0-100°C Automatic/Manual) with accuracy ±0.01.

All the systems were investigated in equimolar condition at three different ionic strengths (*i.e.*, $\mu = 0.05\text{M}$, 0.10M , 0.15M) at $20\pm 1^\circ\text{C}$ and $30\pm 1^\circ\text{C}$ in aqueous medium. NaNO₃ was used as background electrolyte. All the sets of titration mixture were prepared same as described elsewhere[16], and titrated with carbonate free 0.10M NaOH solution.

The results were calculated by algebraic method of Chaberek and Martell[18,19] as modified by Dey *et. al.*[20] and refined by using SCOGS computer program[21-23]. These values were plotted against $\sqrt{\mu}$ and extrapolated to zero ionic strength to obtain thermodynamic formation constants of complexes.

ΔG° , ΔH° and ΔS° were calculated by van't Hoff isotherm, van't Hoff isochore and Gibb's Helmholtz equation. Results are summarized in Table 1 and 2.

TABLE I.

Protonation Constants of Ligands ($\log \beta_{\mu \rightarrow 0}$) and Thermodynamic Formation Constants of Binary Complexes of Coblat(II) in Equimolar Systems

Parameter	Ligand									
	DOPM		Ala		Phe		Asp		Glu	
	20°C	30°C	20°C	30°C	20°C	30°C	20°C	30°C	20°C	30°C
$\log \beta_{\text{HA}}$	12.01	1.70	10.25	10.01	9.31	9.12	10.57	10.26	10.33	10.07
$\log \beta_{\text{H}_2\text{A}}$	22.65	22.05	-	-	-	-	15.05	14.69	14.90	14.54
$\log \beta_{\text{H}_3\text{A}}$	31.65	30.94	-	-	-	-	-	-	-	-
$\log \beta_{\text{MAH}_2}$	26.27	25.64	-	-	-	-	-	-	-	-
$\log \beta_{\text{MAH}}$	17.42	16.96	-	-	-	-	14.53	14.16	14.23	13.92
$\log \beta_{\text{MA}}$	8.45	8.17	6.26	6.20	5.86	5.62	8.40	8.23	7.60	7.44
$\log K_{\text{MAH}_2}^{\text{M}}$	3.62	3.58	-	-	-	-	3.96	3.90	3.90	3.84
$\log K_{\text{MAH}}^{\text{M}}$	5.41	5.27	-	-	-	-	6.14	5.93	6.63	6.48

- Thermodynamic formation constants were obtained by extrapolating the $\log \beta$ vs. $\sqrt{\mu}$ plot to zero ionic strength.
- Ala, Phe, Asp and Glu become the ligand 'B' in ternary systems.

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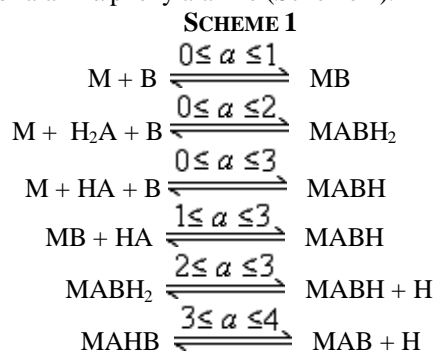
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TABLE 2.
Thermodynamic Formation Constants and Other Thermodynamic Parameters of
Co(II)-DOPM-Ligand 'B' Ternary Complexes in Equimolar Systems

System	Parameter	20°C		30°C		-ΔH° kJmol ⁻¹	ΔS° JK ⁻¹ mol ⁻¹
		logK _{μ→0}	-ΔG° kJmol ⁻¹	logK _{μ→0}	-ΔG° kJmol ⁻¹		
Co(II)- DOPM -Ala	log β _{MABH₂}	32.17	180.48	31.35	181.88	139.39	140.23
	log β _{MABH}	23.60	132.37	22.82	132.42	131.06	4.47
	log β _{MAB}	13.57	76.13	13.14	76.23	73.09	10.36
Co(II)- DOPM -Phe	log β _{MABH₂}	31.53	176.86	30.49	176.91	175.26	5.47
	log β _{MABH}	22.99	128.95	22.23	129.00	127.51	4.92
	log β _{MAB}	12.85	72.09	12.44	72.17	69.69	8.18
Co(II)- DOPM - Asp	log β _{MABH₃}	41.92	235.18	40.92	237.40	169.99	222.49
	log β _{MABH₂}	33.78	189.51	32.94	191.10	142.79	159.46
	log β _{MABH}	24.50	137.45	23.87	138.48	107.09	103.61
	log β _{MAB}	14.15	79.38	13.79	80.00	61.20	62.08
Co(II)- DOPM - Glu	log β _{MABH₃}	41.20	231.14	40.27	233.63	158.09	249.31
	log β _{MABH₂}	32.81	184.07	31.99	185.59	139.39	152.49
	log β _{MABH}	23.49	131.78	22.92	132.97	96.89	119.08
	log β _{MAB}	13.24	74.28	12.89	74.81	58.82	52.77

IV. RESULTS AND DISCUSSION

Titration curves were obtained by plotting pH against 'a' (where, 'a' is the moles of alkali added per mole of metal/ligand). Pattern of experimental curves for the systems of cobalt was identical to the trend of titration curves of Ni(II)-DOPM-Ala/Phe/Asp/Glu systems[15]. Complexation behaviour of ligands was analyzed by examining these curves by using method of Carey and Martell[24]. These analyses reveal that Co(II) ion simultaneously coordinates with both the ligands in the systems of alanine/phenylalanine (Scheme 1).



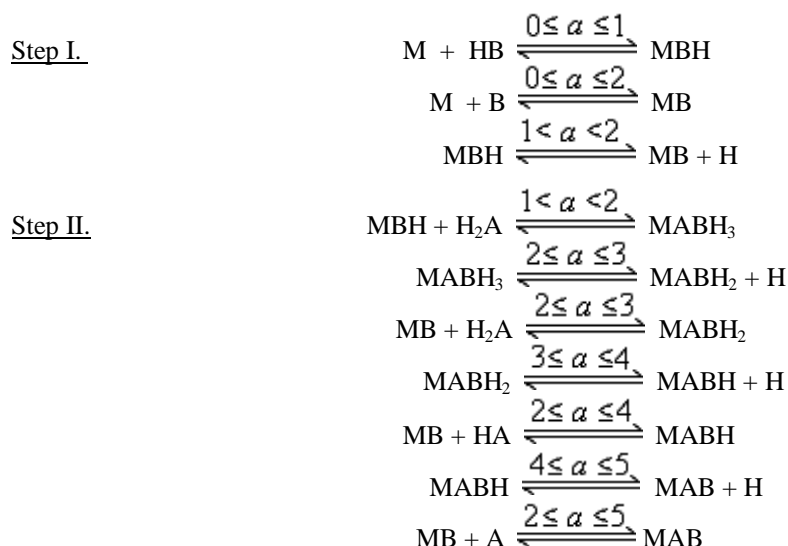
Whereas aspartic acid/glutamic acid coordinate with cobalt in the first step, at comparatively lower pH, and then mixed ligand complex is formed in the second distinct step in Co(II)-DOPM-Asp/Glu systems (Scheme 2).

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SCHEME 2



Percentage distribution of metal in Co(II)-DOPM-Ala/Phe systems (Fig. 1) shows that up to pH 8.5 diprotonated Co(II)-DOPM and Co(II)-Ala/Phe monoligand complexes are formed along with the coexistence of diprotonated biligand complex (Co(II)ABH₂). Above this pH, concentrations of all these species decrease and monoprotated biligand complex, Co(II)ABH, is formed as major biligand complex up to pH 9.5, consuming about 50% of metal ion, supporting coordination of dopamine through pyrocatechol site with protonated amine group[25].

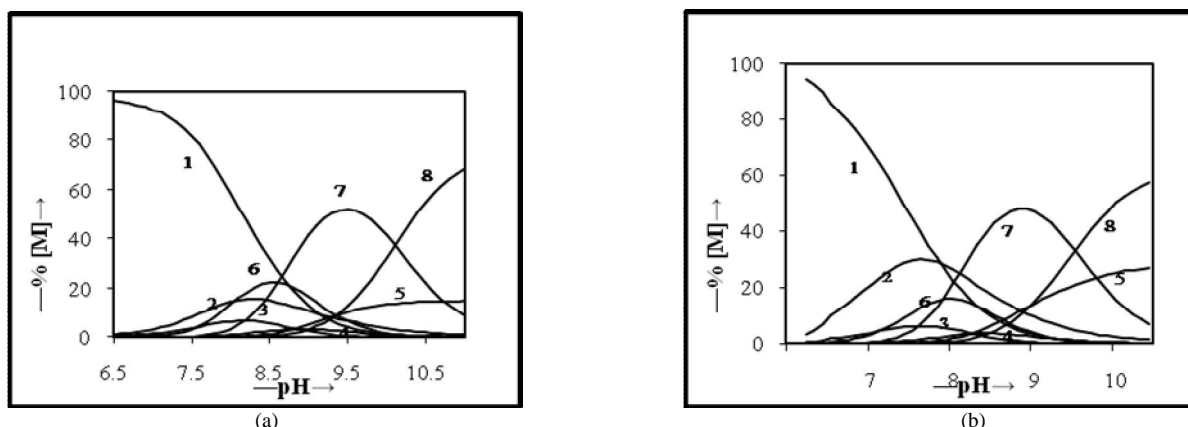


Fig. 1. Speciation Curves for (a) Co(II)-DOPM-Ala and (b) Co(II)-DOPM-Phe (1:1:1) System at 20±1°C (m=0.10M (NaNO₃))
Where, Curve 1 : [M]; 2 : [MB]; 3 : [MAH₂]; 4 : [MAH]; 5 : [MA]; 6 : [MABH₂]; 7 : [MABH]; 8 : [MAB]

Then At higher pH (>10.0) metal is distributed in Co(II)A, Co(II)ABH and Co(II)AB. Nature of curves support formation of nonprotonated biligand complex by combination of Co(II)B complex with ligand 'A' up to pH 9.5 and then only by dissociation of monoprotated biligand complexes(Co(II)ABH). As the concentration of Co(II)A remains constant in the higher pH region disproportionation reaction doesn't contribute to the formation of Co(II)AB complex (scheme 1).

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In the systems of phenylalanine concentration of biligand complexes is comparatively low with increased concentration of Co(II)A type complex at the end. That is due to hydrophobic nature of phenyl ring of phenylalanine, which tends to aggregate in the solution at higher pH. The two steps involved in the systems of Asp and Glu are shown in Scheme 2). Speciation curves for Co(II)-DOPM-Asp/Glu (1:1:1) systems (Fig. 2) support this stepwise equilibria as was predicted from titration curves[15].

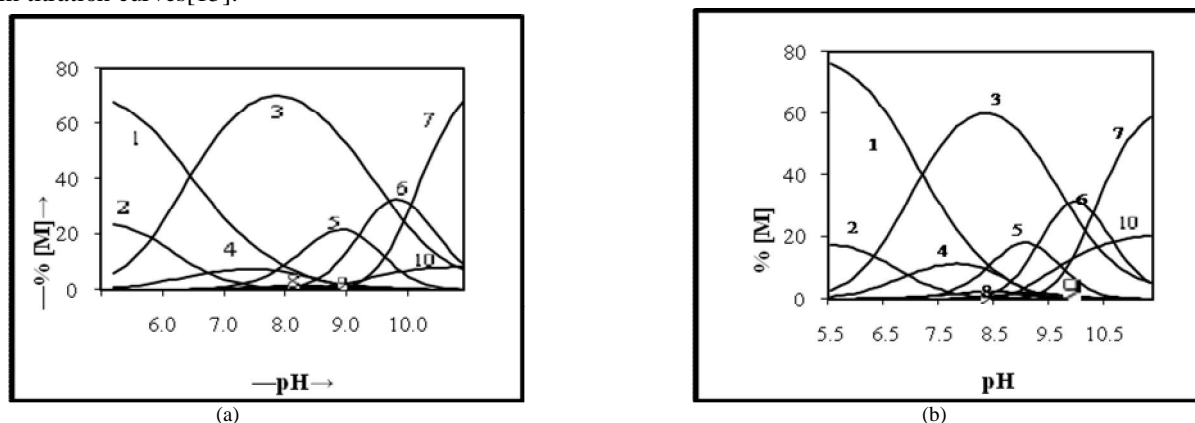
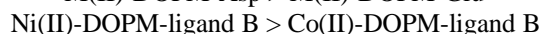
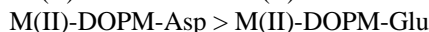
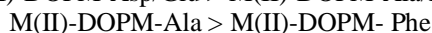
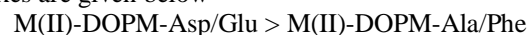


Fig. 2 Speciation Curves for (a) Co(II)-DOPM-Asp and (b) Co(II)-DOPM-Glu (1:1:1) System at $20 \pm 1^\circ\text{C}$ ($m=0.10\text{M}$ (NaNO_3))
 Where, Curve 1 : [M]; 2 : [MBH]; 3 : [MB]; 4 : [MABH₃]; 5 : [MABH₂]; 6 : [MABH]; 7 : [MAB]; 8 : [MAH₂]; 9 : [MAH]; 10 : [MA]

Here aspartic acid/glutamic acid behaves as primary ligand. In these systems monoprotonated and nonprotonated Co(II)-Asp/Glu complexes (*e.i.* Co(II)BH and Co(II)B) are formed as dominating species up to pH 8.0, consuming about 70% of metal. Consequently, concentrations of monoligand complexes of Co(II) with dopamine (Co(II)AH₂, Co(II)AH and Co(II)A) were found to be very low or negligible. Co(II)BH undergoes dissociation forming Co(II)B above pH 5.0 and almost disappeared up to pH 7.5, at which Co(II)ABH₂ starts forming. Clearly all the protons in biligand complexes, except Co(II)AH₃, are associated with dopamine site only[25]. Co(II)ABH₂, Co(II)ABH and Co(II)AB complexes are formed by combination of Co(II)B with ligand 'A' (with corresponding protonation) as well as by dissociation of higher protonated species in overlapping equilibria, which was well expected as no sharp inflection was observed in biligand titration curve after ' α ' = 2. Dopamine coordinates with metal ion in pyrocatechol mode and all the other ligands bind with metal in glycine like mode[25].

V. CONCLUSION

Stability orders of complexes are given below –



Complexes of aspartic acid/glutamic acid are more stable because of formation of additional chelate ring than Co(II)-DOPM-Ala/Phe complexes. Stability of glutamic acid complexes is lower in comparison to aspartic acid complexes, which is due to additional –CH₂– group in the side chain of former ligand, reducing stability, by forming 7-membered chelate ring.

In case of Co(II)-DOPM-Ala systems, decreased stability of complexes of phenylalanine is attributed to electron withdrawing nature of phenyl ring of particular ligand and repulsion between bulky side groups of two ligands. The complexes of nickel[15] and cobalt follow the Irving-Williams stability sequence[26].

Cobalamin is necessary for maintenance of the nervous system[27] and all the selected ligands also play vital role in CNS[3,4]. Hence these studies are helpful in understanding physiology of cobalt with neurotransmitters.

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REFERENCES

- [1] L. Lamarque, P. Navarro, C. Miranda, V.J. Aran, C. Dchoa, F. Escarti, E. Garcia-Espana, J. Latorre, S.V. Luis & J.F. Miravet, J. Am. Chem. Soc., vol. 123, No. 43, 10560, 2001.
- [2] T.V. Pathak, J.P. Mehta, P.N. Bhatt & G. Ramachandraiah, Trans. SAEST, vol. 38, No. 3, 107, 2003.
- [3] P.J. Reeds, *et. al.*, "Intestinal Glutamate Metabolism", J. Nutrition, vol. 130, No. 4S, 978S, 2000.
- [4] D. Voet, J.G. Voet & C.W. Pratt., "Fundamentals of Biochemistry Upgrade Edition", John Wiley & Sons, Inc., 656, 2001.
- [5] G. Jaouen, Ed. Bioorganometallics: Biomolecules, Labeling, Medicine; Wiley-VCH: Weinheim, 2006.
- [6] K. Kumar, D.K. Dwivedi, IJRSET, vol. 3, No. 7, July 2014.
- [7] M. Devi, R. Nair(Ahuja), Int. J. Sci. Res. (IJSR), vol. 4, No. 4, April, 2015.
- [8] M. Devi, R. Nair(Ahuja), IOSRJ Appl. Chem., vol. 8, No. 13, 52, 2015.
- [9] T. Kiss, I. Sóvágó & R.B. Martin, J. Am. Chem. Soc., vol. 111, 3611, 1989.
- [10] M.S. Nair & M. Santappa, Indian J. Chem., vol. 20(A), 990, 1981; J. Chem. Soc., Dalton Trans, 992, 1981.
- [11] M.S. Nair, K.V. Chalapathy, P.K. Murugan & M. Santappa, Inorg. Chem., vol. 21, 2418, 1982; J. Chem. Soc., Dalton Trans., 55, 1982.
- [12] D. Chdraborty & P.K. Bhattacharya, J. Chem. Soc., Dalton Trans, 3225, 1990.
- [13] M.S. Nair, P.T. Arasu, S.S. Mansoor, P. Shenbagavatti & M.A. Neelkantan, Indian J. Chem., vol. 34(A), 365, 1995.
- [14] M.S. Nair, P.T. Arasu & M.A. Neelkantan, Indian J. Chem., vol. 36(A), 879, 1997.
- [15] Neerja Dwivedi, K. Dwivedi & R. Nair (Ahuja), Orient. J. Chem., vol. 24, No. 2, 521, 2008.
- [16] Neerja Upadhyaya (Dwivedi), K. Dwivedi & R. Nair (Ahuja), J. Indian Chem. Soc., vol. 86,252, 2009.
- [17] S.K. Yadav, N. Upadhyaya (Dwivedi), K. Dwivedi & R. Nair (Ahuja), J. Indian Chem. Soc, vol. 88,1599.,2011.
- [18] S. Chaberek & A.E. Martell, J. Am. Chem. Soc., vol. 74, 5052, 1952.
- [19] S. Chaberek & A.E. Martell, J. Am. Chem. Soc., vol. 77, 1477, 1955.
- [20] Ram Nayan & A.K. Dey, Indian J. Chem., vol. 14(A), 892, 1976.
- [21] I.G. Sayce, Talanta, vol. 15, 1397, 1968.
- [22] I.G. Sayce, Talanta, vol. 18, 653, 1971.
- [23] I.G. Sayce & V.S. Sharma, Talanta, vol. 19, 831, 1972.
- [24] G.H. Carey & A.E. Martell, J. Am. Chem. Soc., vol. 89, 9895, 1967.
- [25] M.S. Nair & G. Subbalakshmi, J. Indian Chem. Soc., vol. 77, 26, 2000.
- [26] H. Irving & R.J.P. Williams, J. Chem. Soc., vol. 5, 3192, 1953.
- [27] H. Sigel, A. Sigel & K.O. Ronald Sigel, "Metal ions in life science", John Willey & Sons Ltd., Chichester, U.K.,44, 2006.