ISSN: 2583-0236 BIGYAN **1**, 5 (2021)

Synthesis and characterization of Mn (II), Co (II) and Cu (II) complexes with tetradentate N_2O_2 donor Schiff Base: interaction with human serum albumin (HSA) with Cu(II) complex

Animesh Patra[1*], Surajit Maiti[1], Soumyakanti Maity[1] and Aesha Das[1]

[1]Postgraduate Department of Chemistry, Midnapore College, Midnapore- 721101, India

Abstract

A tetra coordinated manganese(II), cobalt(II) and copper(II) complexes formulated as [Mn(L] (1), [Co(L)](2) and [Cu(L)](3) H_2Lwere synthesized and characterized by elemental, physico-chemical and spectroscopic methods. The four coordination spheres of metal (II) ions have been satisfied by two imine nitrogen- N and two phenolate oxygen-O donors of organic moiety (H_2L). The electrochemical study revealed that copper (II) complex is a quasi-reversible one-electron transfer process. The interaction of copper (II) complex with human serum albumin (HSA) was examined with the help of absorption spectroscopic tools. From this study which suggested that copper (II) was strongly interaction with Human serum albumin (HSA) protein.

Keywords: Transition metal complexes; Schiff base; Binding with HSA, Electrochemical study

1. Introduction

Complexes of Schiff base ligand have been studied for their dioxygen untaken [1-3] and oxidative catalysis [4]. Schiff base complexes have important properties, e.g., ability to bind toxic and heavy metal atoms, undergo tautomerism [4], exhibit catalytic reduction and photochromism. The basic strategy to design such materials is to organize paramagnetic centres into poly nuclear aggregates or polymeric networks by use of bridging ligands that can efficiently propagate magnetic super exchange. Several studies have also shown that diazo compounds exhibit properties similar to those of Schiff bases [5]. Napthylamine-derived azo-linked Schiff bases and their metal complexes have additional applications, especially in the dye industry. The role of the metal– Schiff base complexes in such applications is related to molecular structure. Thus, it is quite important to have a good understanding of the structure of such metal complexes [6].

Human serum albumin is collected of three homologous domains (I, II and III), each containing A and B. Each domain contains subdomains A and B. Aromatic and heterocyclic ligands are found to bind within two hydrophobic pockets in subdomains IIA and IIIA, described as site I and site II [7,8]. Human serum albumin plays an chief role in osmotic pressure, pH of blood and various biological functions [9].

In this respect, present study aimed to investigate the reaction of tetra dentate Schiff bases derived from the condensation of 2-Hydroxy napthaldehyde with 4-nitro 1,2-diamino benzene. The complexes are prepared by the equimolar ratio of ligand with metal (II) acetate. The interactions of copper (II) complex towards human serum albumin (HSA) were examined with absorption spectroscopic tools.

2. Experimental methods

2.1. Materials and Physical measurements:

Starting materials are obtained from commercial sources. Molar conductance's (Λ_M) were measured in a systronics conductivity meter 304 model using ~10^{-3} mol.L^{-1} solutions in appropriate organic solvents. The stock solutions of protein (1.00×10^{-4}mol L^{-1}) was prepared by dissolving the solid HSA in 0.05 M HEPES buffer at pH 7.4 and stored at 0−4 °C in the dark. Cyclic voltammetry were recorded using ELECTROCHEMICAL ANALYSER MODEL CHI600E.

2.2. Preparation of the ligand (H_2L)

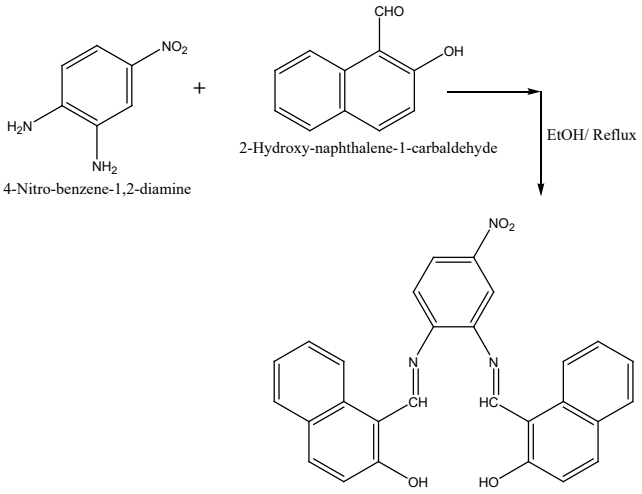
The ligand **H_2L** was Synthesize by adding 2.064 g (12.0 mmol) of 2-Hydroxy naphthaldehyde and then 0.9188 g (6.0 mmol) of 4-nitro 1,2-diamino benzene with 10 mL of ethanol in a round bottom flask with magnetic stirring given in **Scheme 1**. Stir the solution for 3 hour and then reflux up to 2 hour and kept overnight to get the precipitate of the orange solid ligand and finally crude product was collected by recrystallization in ethanol and dried the solid product as much as possible, Yields >80%.

2.3. Preparation of [Mn(L)] (1) , [Co(L)] (2) and [Cu(L)] (3)

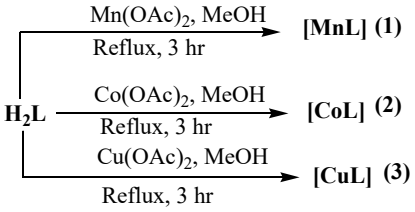
E-mail: animeshpatramc@gmail.com

Received 30/05/2021, Accepted for publication 02/08/2021. Published

To prepare these complexes (**1,2 and 3**) a common procedure was followed as described below, using manganese acetate for complex (**1**) and cobalt acetate for complex (**2**) and copper acetate (**3**) the organic ligand (**H_2L**) in equimolar ratio (1:1), shown in **Scheme 2**. A methanolic solution of **H_2L** was mixed with 1.0 mmol of metal acetate in methanolic solution with stirring condition, and the mixture was refluxed for 4 h. Then filter and dried in vacuo.



Scheme 1: Synthetic procedure for the preparation of Ligand (**H_2L**)



Scheme 2. Synthetic strategy of the Mn (II), Co(II) and Cu(II) complexes

2.4. Protein (HSA) binding experiments

The quantitative analyses of the interaction between Cu(II) complex and human cerum albumin were performed by absorption spectroscopic titration[10]. A 3.0 mL portion of aqueous solution of protein was titrated by gradual addition of the appropriate concentration of Cu (II) complex solution (to give a final concentration of 3.8×10^{-6}mol L^{-1}). For every addition, the solution mixture was shaken and allowed to stand for 10 minute, and then the absorption spectra were measured.

3. Results and Discussions

3.1. Synthesis and characterization:

The organic ligand **H_2L** was synthesized by the reaction of the respective of 2-hydroxy naphthaldehyde and then 4-nitro 1,2-diamino benzene (2:1) in presence of Ethanol. The complexes were obtained in good yield from the reaction of metal acetate with equimolar amount of respective organic moiety **H_2L** in the methanol medium. The elemental analysis of Ligan and complexes are given in **Table-1**. In these complexes the organic molecule **L** act as tetradentate ligand through N_2O_2- donor centres. The possible arrangement of complexes is given in **Fig. 1**.

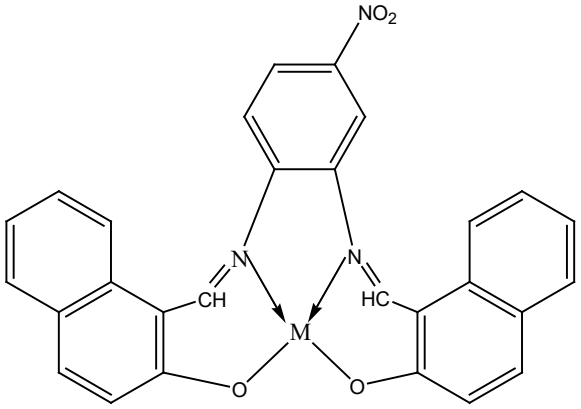


Fig 1. Probable structure of ML complexes **(M = Mn, Co, Cu)**.

3.2. Electrochemistry:

The electrochemistry of the copper (II) complex was examined by cyclic voltammetry (**Fig.2**). From this study, the complex **3** gives reduction peak at E_{pc}= -0.25V and with a corresponding oxidation peak at E_{pa}= 0.71V with a scan rate interval 50–400 mV s^{-1}. The cathodic to anodic ratio peak height was close to one which indicated that the complex is related to a quasi-reversible one-electron transfer process.

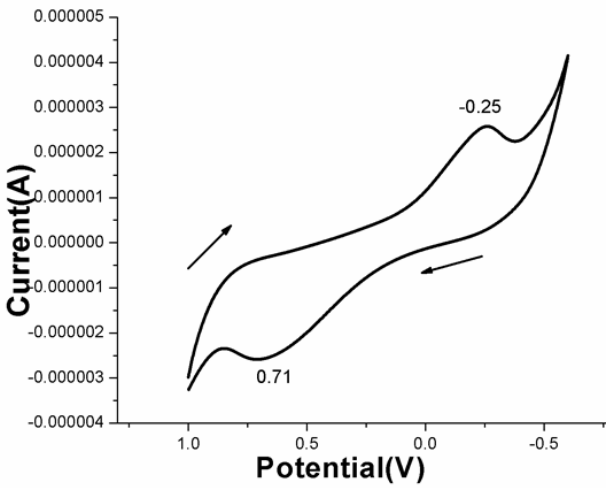


Fig 2 : Cyclic voltammetry curve of cu(II) complex

3.3. Electronic absorption Spectral Study:

The electronic spectra of the ligand and its complexes were recorded in DMF at room temperature **(Fig. 3)**. The spectra of the Schiff base H_2L exhibit three main peaks: at 288.0, 328.0, 550.0 and 640 nm. The first and second peaks were attributed to benzene n→π* and iminoπ→π* transitions, again an absorption band at 550.0 nm and 640 nm are due to intra ligand charge transfer transition. All the spectra of complexes shows lower bands than 400 nm are due to intramolecularπ→π* and n →π* transitions for the aromatic ring.

The Mn-complex shows only high energy bands at 350,450 and 642 nm, which are due to intraligand transitions and lower energy band at 450 nm and 642 are attributed to the L→M charge transfer transition.

Table-1: Elemental Analysis of manganese(II), cobalt(II) and copper(II) complexes**.**

Formula	Compound	Mol.weight	Colour	Calculated Percentage				Melting point
				C	H	N	M	
$C_{28}H_{19}N_3O_4$	L	461	Orange	72.88	4.12	9.11	-	184
$C_{28}H_{19}N_3O_4Mn$	1	516	Brown	65.11	3.68	8.14	10.66	>215
$C_{28}H_{19}N_3O_4Co$	2	520	Brown	64.61	3.65	8.07	11.34	>215
$C_{28}H_{19}N_3O_4Cu$	3	524.5	Chocolate brown	64.06	3.62	8.09	12.10	>215

In cobalt (II) complex, three spin allowed transitions are expected from the energy level diagram for d^7 ion due to $^4A_2 \rightarrow {}^4T_1$ (P), $^4A_2 \rightarrow {}^4T_1$(F), $^4A_2 \rightarrow {}^4T_2$ transitions, which are observed at low to high wavelengths respectively. For cobalt complex bands at 420 nm, 600nm, which may be assigned to $^4A_2 \rightarrow {}^4T_1$(P) and $^4A_2 \rightarrow {}^4T_1$(F) transitionrespectively. Again the intensity of the peak at around 642 nm observed due to the $^4A_2 \rightarrow {}^4T_2$ transition [14].

Copper (II) complex shows peak at 285, 320 and 420 nm. 285 and 320 nm peaks are attributed to intramolecular$\pi \rightarrow \pi^*$ and n $\rightarrow \pi^*$ transitions for the aromatic ring and 420 nm is attributed to d-d and charge transfer transitions.

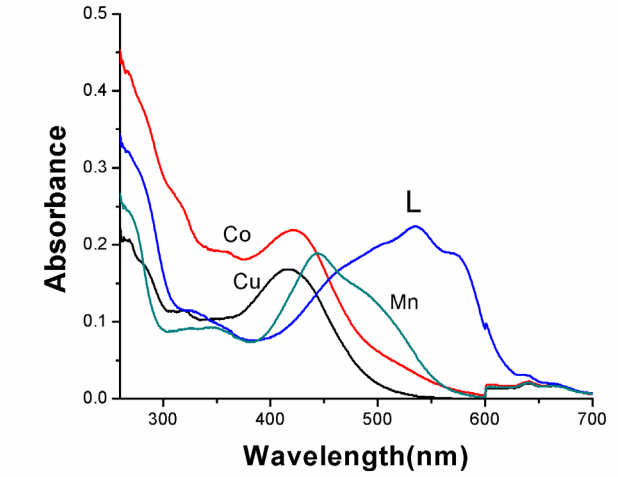


Fig. 3. UV spectra of Ligand and Complexes.

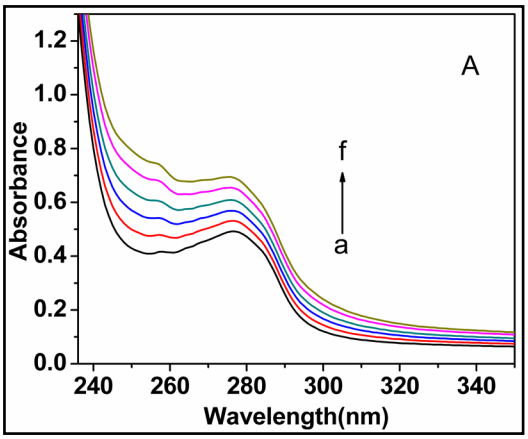


Fig 4. The Electronic spectral titration of complex 3 with HSA in HEPES buffer. Arrow indicates increase the concentration of HSA.

3.4. Absorption characteristics of HSA –Cu(II) complex:

The absorption spectra of HSA in the absence and presence of Cu(II) complex was studied at different concentrations[15]. From this study we observed that absorption of increases regularly upon increasing the concentration of the complex. The absorption spectral data of copper complex with HSA shown in **Fig. 4** From these data the apparent association constant (K_{app}) determined of the complex with HSA has been determined using the Benesi-Hildebrand equation [16]. The value of the apparent association constant (K_{app}) of HSA is 4.28×10^{-4} (R = 0.99897) determined from this plot (**Fig.5**) and represent a good linear relationship [17].

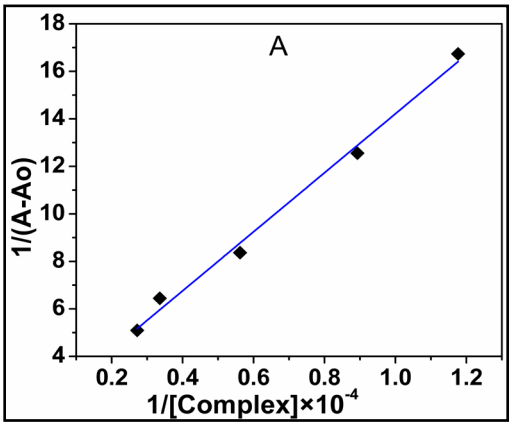


Fig 5. Plot of 1/(A-Ao) vs 1/[Complex 3] resulting from the electronic spectral titration with HSAin HEPES buffer

4. Conclusion

The synthesis and characterized of two mononuclear Mn (II), Cu (II) and Co (II) complexes with a N_2O_2- donor set have been performed. The ligand **H_2L** behaves as a N_2O_2-donors.Melting point experiments show that the synthesized Schiff base complexes exhibit a significant thermal stability. In these complexes metal ions are coordinated to the Schiff base via the phenolic oxygen and the imino nitrogen and all the complexes are distorted square planar geometry. The interactions of copper (II) complexes towards HSA were examined with the absorption spectroscopic tools. The absorption spectral titration indicated that Cu (II) ion strongly binds with HSA protein.The three complexes are characterized by UV–Vis and electrochemical techniques.

Acknowledgements

We are thankfully acknowledging the financial support from RUSA 2.0 component: 8, Memo No.: 620/MC/RUSA-2.0/PROJECT/19/13(12), India. Again we are thankful to Prof.

Pabitra Chattopadhyay, Dept. of Chemistry, Burdwan University, Burdwan, for his encouragement and guidance.

References

1. Adsule S, Banerjee S, Ahmed F, Padhye S, Sarkar FH, Hybrid anticancer agents: isothiocyanateprogesterone conjugates as chemotherapeutic agents and insights into their cytotoxicities. Bioorg.Med.Chem. 2010; 20:1247-1251.
2. Asiri AM, Khan SA, Synthesis and Anti-Bacterial Activities of Some Novel Schiff Bases Derived from Aminophenazone. Molecules, 2010; 15: 6850-6858.
3. Singh WM, Dash BC. Synthesis of some new Schiff bases containing thiazole and oxazole nuclei and their fungicidal activity, Pesticides 1988; 22: 33-37.
4. Sheikh RA, Shreaz S, Sharma GS, Khan LA, Hashmi AA. Synthesis, characterization and antimicrobial screening of a novel organylborate ligand, potassium hydro(phthalyl)(salicylyl)borate and its Co(II), Ni(II), and Cu(II) complexes. J. Saudi Chem. Soc. 2012; 16: 353–361.
5. Raman N, Sobha S, Mitu L. Design, synthesis, DNA binding ability, chemical nuclease activity and antimicrobial evaluation of Cu(II), Co(II), Ni(II) and Zn(II) metal complexes containing tridentate Schiff base. J. Saudi Chem. Soc. 2013; 17: 151–159.
6. Bagihalli GB, Avaji PG, Patil SA, BadamiPS.Synthesis, spectral characterization, in vitro antibacterial, antifungal and cytotoxic activities of Co(II), Ni(II) and Cu(II) complexes with 1,2,4-triazole Schiff bases. Eur. J. Med. Chem. 2008; 43: 2639-2649.
7. Zhang P, Cheetham A G, Lock L L, Cui H. Cellular Uptake and Cytotoxicity of Drug–Peptide Conjugates Regulated by Conjugation Site.Bioconjugate Chem., 2013; 24: 604–613.
8. Dong S, Li Z, Shi L, Huang G, Chen S, Huang T. The interaction of plant-growth regulators with serum albumin: molecular modeling and spectroscopic methods. Food Chem. Toxicol., 2014; 67: 123-130.
9. Xiao CQ, Jiang F L, Zhou B, Li R, Liu Y. Interaction between a cationic porphyrin and bovine serum albumin studied by surface plasmon resonance, fluorescence spectroscopy and cyclic voltammetry.Photochem. Photobiol. Sci. 2011; 10: 1110-1117.
10. Hazra M, Dolai T, Giri S, Patra A, Dey SK. Synthesis of biologically active cadmium (II) complex with tridentate N_2O donor Schiff base: DFT study, binding mechanism of serum albumins (bovine, human) and fluorescent nanowires. J. Saudi Chem. Soc. 2014.
11. Konar S, Jana A, Das K, Ray S, Chatterjee S, Golen JA, Rheingold AL, Kar SK. Synthesis, crystal structure, spectroscopic and photoluminescence studies of manganese(II), cobalt(II), cadmium(II), zinc(II) and copper(II) complexes with a pyrazole derived Schiff base ligand. Polyhedron 2011; 30: 2801-2808.
12. Gaballa AS, Teleb S M, Asker M S, Yalçin E, Seferoğlu Z. Synthesis, spectroscopic properties, and antimicrobial activity of some new 5-phenylazo-6-aminouracil-vanadyl complexes. J. Coord. Chem. 2011; 64: 4225–4243.
13. Siddiqui RA, Raj P, SaxenaAK.Preparation and Structural Characterisation of TriarylMetal(V) Complexes (M = As, Sb) of Tri-and Tetradentate Schiff Bases.Synth. Inorg. Met. Org. Chem. 1996; 26: 1189-1203.
14. Kessel SL, Emberson RM, Debunner PG, Hendrickson DN.Iron(III), manganese(III), and cobalt(III) complexes with single chelating o-semiquinoneligandsInorg. Chem.1980; 19: 1170-1178.
15. Zhang J, Zhuang S, Tong C, Liu W. Probing the molecular interaction of triazole fungicides with human serum albumin by multispectroscopic techniques and molecular modeling.J. Agric. Food Chem. 2013; 61: 7203–7211.
16. Benesi HA, Hildebrand JH. A Spectrophotometric Investigation of the Interaction of Iodine with Aromatic Hydrocarbons. J. Am. Chem. Soc., 1949; 71: 2703–2707.
17. Samari F, Hemmateenejad B, Shamsipur M, Rashidi M, Samouei H. Affinity of two novel five-coordinated anticancer Pt(II) complexes to human and bovine serum albumins: a spectroscopic approach. Inorg. Chem., 2012; 51: 3454-3464.
18. More PG, Bhalvankar RB, Pattar SC. Schiff bases derived from substituted-2-aminothiazole and substituted salicylaldehyde and 2-hydroxy-1-napthaldehyde exhibits antibacterial and antifungal activity. J. Indian Chem. Soc. 2001; 78: 474-475.
19. Raman N, Kulandaisamy A, Shunmugasundaram A, Jeyasubramanian K. Synthesis, spectral, redox and antimicrobial activities of Schiff base complexes derived from 1-phenyl-2,3-dimethyl-4-aminopyrazol-5-one and acetoacetanilide. Transition Met. Chem. 2001; 26: 131-135.