

Biological and Electrochemical Studies of Macrocyclic Complexes of Iron and Cobalt

Vivek Sharma ¹, Vinod Kumar Vashistha ^{1,*} , Dipak Kumar Das ^{1,*} 

¹Department of Chemistry, GLA University, Mathura, 281406 India

*Correspondence: deepak.das@gla.ac.in (D.K.D); vinod.vashistha@gla.ac.in (V.K.V);

Scopus Author ID 57207705690 (DKD); 56470678100 (VKV)

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Abstract: In this work, we synthesized two tetraaza [N₄] macrocyclic complexes of Fe^{III} and Co^{II} metal ions. The synthesized macrocyclic complexes were fully characterized by using various analytical techniques IR, UV-Vis, and MS. The spectral analysis indicated an octahedral geometry for both macrocyclic complexes. The electrochemical behavior was carried out using cyclic voltammetry on the Pt dish (0.031 cm²) electrode. The complexes were shown to have unusual oxidation states for the metal ions. The “heterogeneous electron transfer rate constant” (K^o) was also calculated using “Nicholson and Kochi’s method” and observed in the order: K^o_{Co^{II} > K^o_{Fe^{III}}. The antimicrobial activities of two complexes were computed against *E. coli*, *P. aeruginosa*, *B. cereus*, *S. aureus*, whereas antifungal activities against *C. Albicans* and were contrasted with the standard drug “Gentamycin”.}

Keywords: Biological activity; macrocyclic complex; electrochemical studies; cyclic voltammetry.

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1. Introduction

Recent advancements in macrocyclic chemistry have allowed synthetic materials for their engineering and to determine their properties [1,2]. While designing innovative new materials, scientists have managed to overcome delicate microstructures. There has risen considerable advancement in the application of combined-valence macrocyclic substances, particularly the emergence of the electronic structure of the classification conceived by researchers through their conceptual study. Transition metal complexes of metals like iron, cobalt, nickel, and copper, etc. have been reported to be very significant for their electrochemical, biological, electronic, and catalytic properties [3-5]. In recent years, studies on the biological activity of diverse types of material have gained much attraction in the development of new macrocyclic complexes of transition metals [6-10]. Diverse properties of transition metal complexes are dependent on the type of substituents present in the ligand structures [11-14]. For instance, the properties of macrocyclic complexes of iron are greatly affected by electronic transfer during the complexation. The considerable functions performed by transition metals in biological systems depend on the containment within virtually planar tetradentate fully closed macrocyclic frameworks that are conjugated systems in their nature itself [15-17]. The synthetic macrocyclic complexes are capable of mimicking the characteristics of naturally produced macrocyclic structures. Therefore, keeping such a view, we synthesized two macrocyclic complexes Fe^{III} and Co^{II} metal ions with the macrocyclic ligand. Further, the synthesized macrocycles were investigated for their electrochemical and biological (antimicrobial and antifungal) activities.

2. Materials and Methods

2.1. Chemical and Reagents.

The elemental analysis of the two macrocyclic complexes was carried out using “Eager Xperience”. Mass spectra of two complexes were recorded on “Mass spectrometer: TOF MS ES+6018e3”. The molar conductance of the complexes was evaluated on “Auto-ranging Conductivity/TDS Meter (TCM 15+)”. The electronic and IR spectra of these macrocyclic complexes were recorded on “Double Beam Spectrophotometer: Shimadzu 2450 spectrophotometer” in methanol and “Shimadzu-8400S double beam spectrophotometer”, respectively. The electrochemical measurements of the macrocyclic complexes were carried out on the Pt electrode (0.031 cm²) using “Auto lab Metrohm 663 VA Stand Instrument”. Tetraethylammoniumperchlorate (TEAP) used as supporting electrolytes.

2.2. Preparation of the Macrocyclic complexes.

The synthesis of macrocyclic complexes (Fig. 1) was conducted by employing 2 moles of 3,4-diaminomethoxybenzene (0.244 g), 2 moles of benzyl (0.422 g), and 1 mole of iron (III) chloride (0.164 g) as per the literature reports [18,19]. The synthesized macrocyclic complexes were characterized using elemental analysis, UV-Vis spectroscopy, IR, and mass spectrometry. The physical parameters of tetraazamacrocyclic complexes of Fe^{III} (A) and Co^{II} (B) are shown in Table 1.

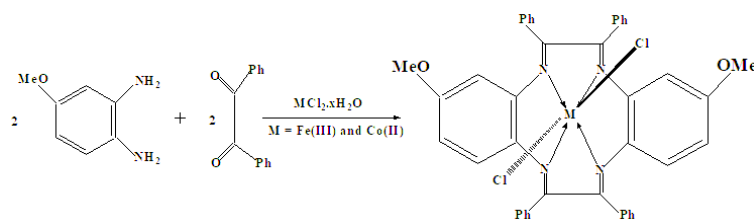


Figure 1. The synthesis scheme of the macrocyclic complexes.

2.3. Biological activity.

The antimicrobial activity of such Fe^{III} and Co^{II} macrocyclic complexes was investigated using the "agar well diffusion method" [21]. Case of fungus, the inhibition zone was evaluated at 25°C after two days of incubation.

Table 1. Physical parameters of tetraazamacrocyclic complexes of Fe^{III} and Co^{II}.

Complexes	Colour	Molar conductance (ohm ⁻¹ cm ² mol ⁻¹)	M.P. (°C)	Mol. Wt.	C (found) (%)	H (found) (%)	N (found) (%)
A- [FeC ₄₂ H ₃₂ N ₄ O ₂ Cl ₂]	Light yellow	768	218	754.7	67.13 (67.17)	4.29 (4.42)	7.43 (7.21)
B- [CoC ₄₂ H ₃₂ N ₄ O ₂ Cl ₂]	Brown	29	220	721.6	66.85 (66.91)	4.27 (5.18)	7.43 (7.31)

The microbe cultures for such macrocyclic complexes have been fixed to 0.5 Mcfarland standards that are conceptually equivalent to a suspension of about 1.5 x 10⁸ CFU/ml for microorganism's bacterium. Then 30 ml of agar media were put into the Petri dishes, as well as the test microbes were swabbed with 100 µl of microorganism's inocula and retained for 25 minutes. At the center of all agar plates, a 6 mm well was slashed and packed with test complexes. The solvent medium was considered as "negative control" while Gentamyci was

employed as a positive control. Incubation after one day at 35°C, every plate has been ascertained for inhibition zone diameter, and in the

3. Results and Discussion

3.1. IR spectra.

The IR spectra of the two complexes displayed a broad peak in the range 1620-1650 cm^{-1} that maybe because of the C=N group in the complexes. The different characteristics peaks for two macrocyclic complexes described in the range 1230-1370 cm^{-1} , 1050-1260 cm^{-1} , 690-890 cm^{-1} , and 2848-2860 cm^{-1} may be allocated for C-H stretching of aromatic moieties and methoxy groups. Also, an absorption band observed in the range 520-490 cm^{-1} could be allocated to $\nu(\text{M-N})$ stretching. The IR spectral data for the complexes are provided in Table 2.

Table 2. IR spectral data of tetraazamacrocyclic complexes of Fe^{III} and Co^{II}.

Macrocyclic complexes	>C=N stretching (cm^{-1})	C=C str. (Aromatic) (cm^{-1})	C—H str. (Methoxy) (cm^{-1})	M—N stretching (cm^{-1})
A	1628	1230, 1028, 796	2848	490
B	1650	1280, 1147, 876	2860	510

3.2. Electronic spectral studies.

The UV-Vis spectral analysis of two complexes was performed in methanol. The data obtained for the complexes are presented in Table 3. Based on the outcome, both macrocycles (A and B) were found to possess “octahedral geometry”. The analyses of the “ligand field parameters” of the macrocyclic complexes (Dq , B' and β) were determined by utilizing "Orgel energy and Tanabe-Sugano" diagrams using a ratio ν_3/ν_1 and ν_2/ν_1 . Using the correlation, the "Nephelauxetic parameter" (β) was evaluated. $\beta = B'/B$ for Fe^{III} = 0.78 and Co^{II} = 0.84 [22]. The computed values of “Ligand Field Parameters” of the complexes are given in Table 3.

Table 3. Electronic spectral data of macrocyclic complexes of Fe^{III} and Co^{II}.

Complexes	Electronic Spectra		Stereo-chemistry	Ligand Field Parameter			
	Energy (cm^{-1})	Transition		Dq (cm^{-1})	ν_3/ν_1	B' (cm^{-1})	β
A	26980	${}^5T_{2g}(\text{D}) \rightarrow {}^5E_g(\text{D})$	Octahedral	1743	1.42	1044	0.78
B	15640 14565 23340	${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{2g}(\text{F})$ ${}^4T_{1g}(\text{F}) \rightarrow {}^4A_{2g}$ ${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{1g}(\text{P})$	Octahedral	970	1.61	964	0.84

3.3. Mass Spectra.

The mass spectra of the complexes A and B revealed the molecular ion peaks (M+1) at m/z 752 and 754, respectively, that can be attributed to the formation of the respective metal complexes. Other peaks noted at m/z 650-670 and 615-655 can be attributed to the cleavage of units -OCH₃ and -Cl, respectively.

3.4. Electrochemical studies.

Electrochemical analysis of both MN₄-macrocycles (M=Fe^{III} and Co^{II}) was conducted using cyclic voltammetry in DMSO having 0.1M triethylamine perchlorate (TEAP) as assisting electrolyte. The CVs (cyclic voltammograms) of both macrocycles are displayed in Fig. 2.

Further, the “diffusion coefficient” (D_0) and “heterogeneous electron transfer rate constant” (K_0) were evaluated using “Nicholson and Kochi’s method” for both macrocycles [23,24]. The CV (Fig. 2a) of FeN₄-complex demonstrated two anodic peaks and one cathodic peak at -0.73 V and -0.32 V and -0.48 V, respectively. Therefore, the first redox process (Fe⁺²/Fe⁺¹) can be attributed to the quasi-reversible redox pair with the peak separation of -0.07 V and formal potential $E_{1/2} = -0.95$ V at 200 mVs⁻¹ scan rate. The quasi-reversibility is also endorsed peak current ratio (i_{pa}/i_{pc}) close to unity. Whereas the second oxidation peak is due to the normal ligand oxidation process.

The CV (Fig. 2b) of the CoN₄-complex indicated a quasi reversible Co^{II}/Co^{III} redox pair contributing to the peak separation of -0.18 V at 200 mV s⁻¹. The redox system is the "quasi reversible process", as also demonstrated by the i_{pa}/i_{pc} peak current ratio. The “heterogeneous electron transfer rate constant” (K^0) was calculated using “Nicholson and Kochi’s method” and observed in the order: $K^0_{Co^{II}}$ (5.31×10^{-3} cm/s) > $K^0_{Fe^{III}}$ (3.47×10^{-3} cm/s). Similarly, The diffusion coefficient (D_0) for both macrocycles was found in the order; $D_0^{Co^{II}}$ (2.25×10^{-5} cm²/s) > $D_0^{Fe^{III}}$ (1.64×10^{-5} cm²/s).

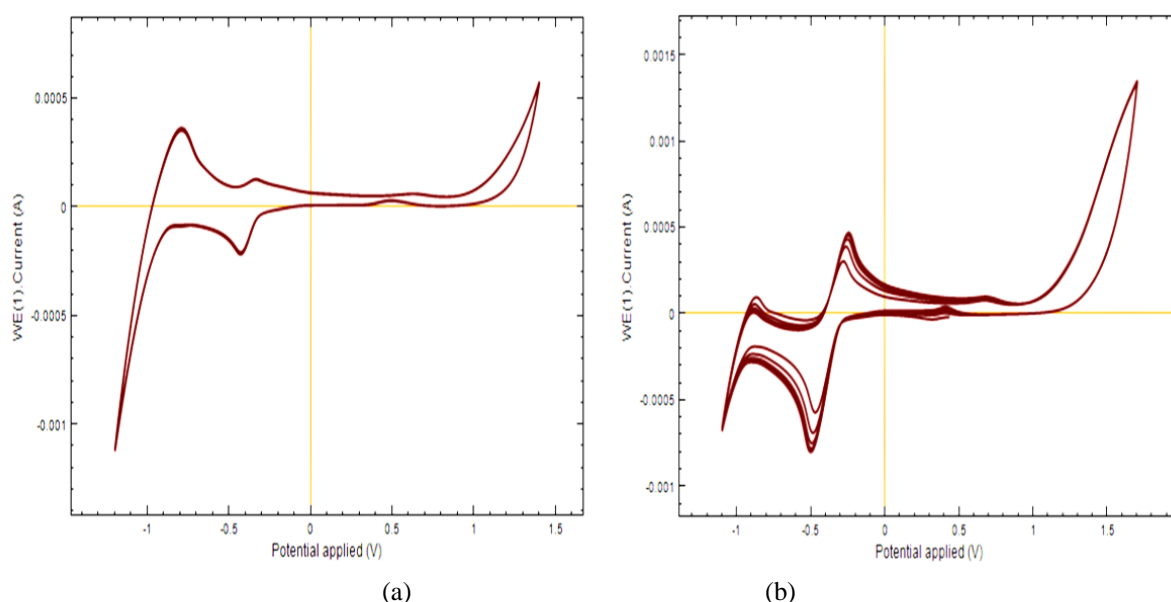


Figure 2. The CV plots of A, and B complexes.

Table 4. Antimicrobial activity of the synthesized macrocyclic complexes.

Complex (100 mg/mL)	Diameter of the inhibition zone (mm)				
	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>B. subtilis</i>	<i>S. aureus</i>	<i>C. Albicans</i>
A	19	16	12	17	19
B	22	15	14	13	16
Gentamycin	26	22	21	24	21

3.5. Biological activity.

Antimicrobial activity of both macrocycles (A and B) was assessed by determining the growth inhibition zone against the model species with zone-reader (Hi Antibiotic Zone Scale) [25]. Complex B exhibited the highest inhibition zone toward *E. coli* (22 mm), and *S. aureus* (15 mm), *B. subtilis* (14 mm), and *P. aeruginosa* (15 mm). While complex A exhibited the highest inhibition zone toward *E. coli* (18 mm), and *B. subtilis* and *S. aureus* (19 mm). *P. aeruginosa* (15 mm), *S. aureus* (14 mm). For antifungal activity against pathogens such as *C. Albicans*,

complex A was observed to be more efficient (19 mm) over the complex B (16 mm), as shown in Fig. 3 and presented in Table 4.

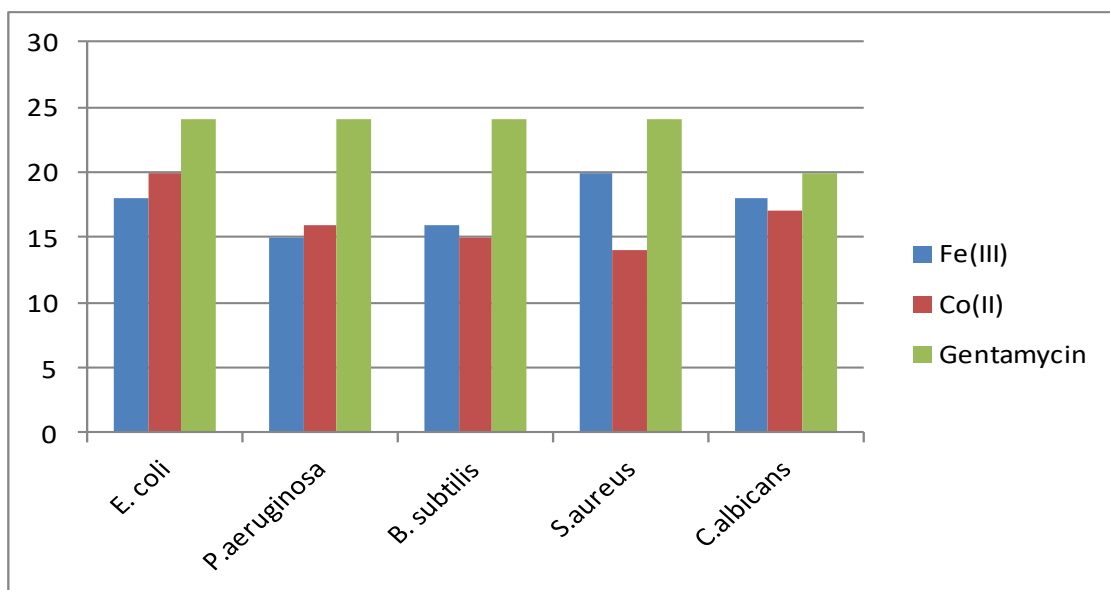


Figure 3. Graphical representation of the antibacterial activities of both macrocyclic complexes against pathogens.

4. Conclusions

In this work, the template synthesis of complexes of Fe^{III} and Co^{II}, utilizing 3,4-diaminomethoxybenzene toluene and benzil, was conducted. The electronic spectral studies have indicated an “octahedral geometry” for both complexes. CV measurements indicated the exciting findings for their uncommon oxidation state. The macrocyclic complexes have displayed promising biological activities against both Gram-positive and Gram-negative bacteria.

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Conflicts of Interest

The authors declare no conflict of interest.

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