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Research Article

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Synthesis, Electrocatalytic Behavior and Biological Evaluation of Trimetallic Macrocyclic Complex with Two Different Bridging Ligands

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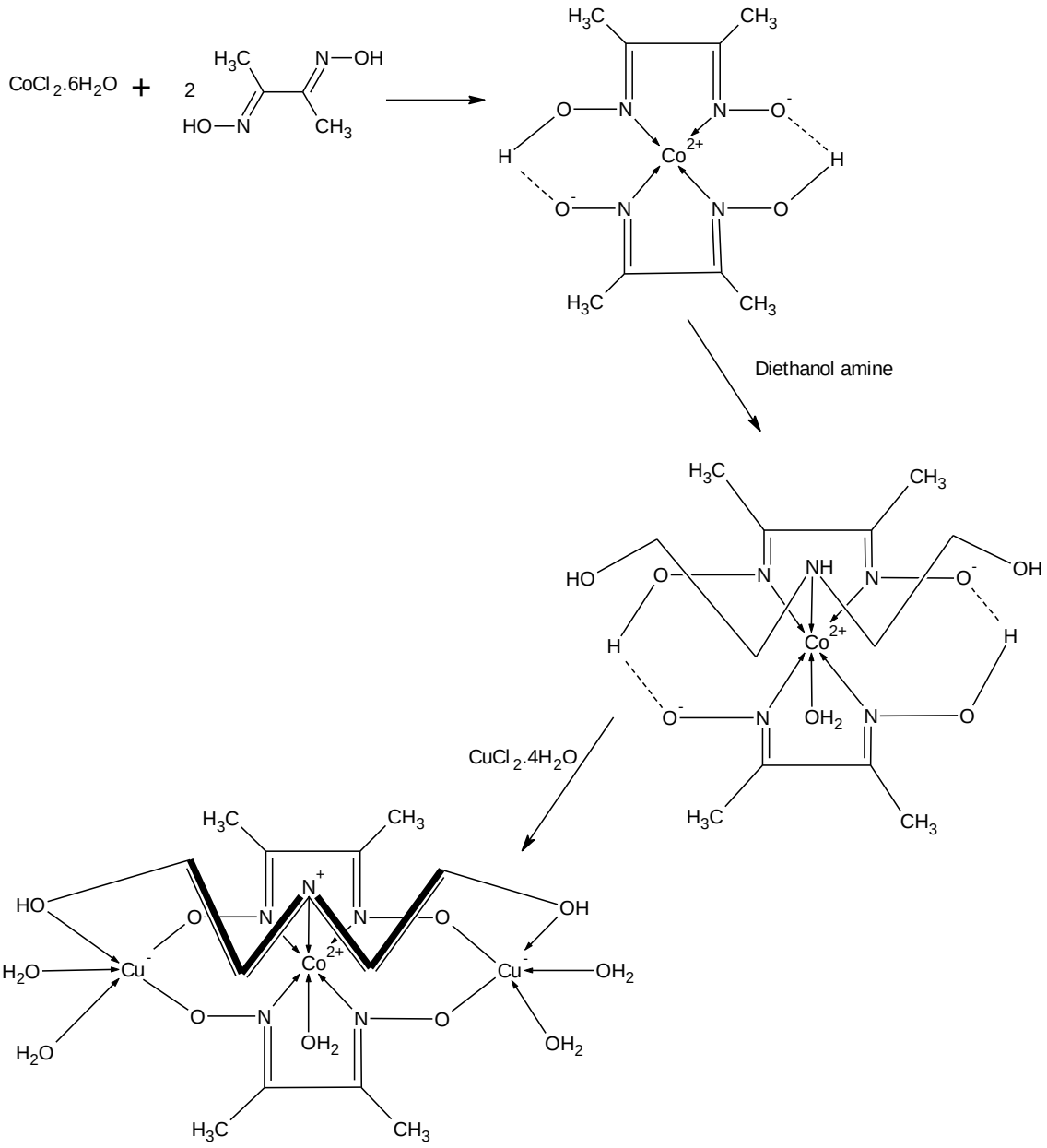
Abstract: This work presents the synthesis and electrocatalytic behavior of unique heterometallic macrocyclic complexes derived from deprotonated cobalt dimethylglyoxime with axially bridged diethanolamine. The electrocatalytic behavior of macrocyclic complexes was tested by cyclic voltammetry and chronoamperometry. Multi-electron, reversible, diffusion controlled and metal-based reduction properties of the complexes show possible application of the complexes as an electrocatalyst for hydrogen evolution in aqueous as well as non aqueous solution. The complexes are easily electro-deposited on the glassy carbon electrode during the repetitive cycles, a very useful feature, for application in fabrication of thin films. Electrocatalytic activities change irregularly with the pH of the solution. Moreover, the catalytic activity of the complexes enhanced significantly, when the complexes were incorporated into the Nafion polymeric matrix as it decreases the overpotential of hydrogen evolution reaction on the glassy carbon electrode up to 0.32 V with augmenting hydrogen discharge current. The complex was screened on *Candida albicans* ATCC 90028 by determining MICs (Minimum inhibitory concentrations) and inhibition in solid media (Disc diffusion assay).

Keywords: Dimethylglyoxime, Coordination polymer, Electrocatalyst, Hydrogen overpotential, Electro-deposition, *Candida albicans* ATCC 90028, MICs.

1. INTRODUCTION

The future of energy supply depends on innovative design of cheap, sustainable and efficient systems for conversion and storage of renewable energy sources. The production of hydrogen through water splitting seems a promising solution for sustainable energy cycles that minimize carbon dioxide emissions [1], but running reaction electrolytically is challenging as it involves two separate multielectron redox processes, a four electron oxidation and a two electron reduction [2]. Also the use of precious metals as electrodes to perform both the hydrogen evolution reaction (HER) and the oxygen evolution reaction (OER), impedes their implementation on a global scale [3-14]. Since the electron or hole



Scheme 1: Schematic representation of synthesis of complex

transfers directly to water and produces extremely high energy intermediates, therefore the process requires catalysts to avoid formation of these species [15, 16]. Despite the recent advances in this field, the design of catalysts with high activity and stability in aqueous media at minimum overpotential is a real challenge [18]. Most of the previously described hydrogen producing systems are biomimetic metal - sulphur clusters that mimic the hydrogenase enzyme [19], imines and clathrochelates [20], cobalt and nickel metallocenes and phosphenes [21] as well as cobalt oximes [22]. The mechanistic studies suggested that the proton reduction in these systems involves electron transfer from electrochemically generated reactive cobalt (I) species. Due to unfavorable thermodynamics of this electron transfer, the resulting overpotential decreases rate of catalysis [23]. One of the possible ways to decrease the overpotential of proton reduction and to make this process thermodynamically favorable is variation of

substituent at dioxamate fragments of the cage ligands. This allows tuning of the potentials of the metal centered redox process [24]. As a result, the potential of electrocatalytic hydrogen production can be controlled. Therefore it is possible to design suitably substituted cobalt dimethylglyoxime complexes that electrocatalyze the proton reduction at potential close to 0 V vs. RHE in this system.

In this work, we report the electrochemical and electrocatalytic behavior of newly synthesized binuclear trimetallic macrocyclic complex derived from cobalt dimethylglyoximate with axially bridging diethanolamine. Furthermore, the catalysts showed both hydrogen evolution and oxidation, confirming their low overpotential for hydrogen production.

2. EXPERIMENTAL SECTION

2.1 Materials and Methods

All the chemicals were of AR Grades and used without further purification. Elemental analyses (percentage of carbon, hydrogen and nitrogen) were performed using a Vario EL elemental analyzer. Infrared spectra (4000-400 cm^{-1}) were recorded at 25^0C using a Perkin Elmer 1750 FTIR spectrophotometer (CT 06859 USA) using KBr pellets in the range of 4000-400 cm^{-1}. Electronic spectra (200-1200 nm) were obtained at 25^0C using a Perkin Elmer Lambda-40, double-beam UV-Visible spectrophotometer, where water was used as medium as well as reference. Cyclic voltametry was carried out on Cyclic voltammetry (CV) was performed using an Autolab Potentiostat/Galvanostat 302N instrument Cyclic voltammeter using three electrode system.

Stock cultures of the microorganisms were maintained on nutrient agar slants and stored at 4°C. *Candida albicans* ATCC 90028 was grown in YPD media respectively at 37 ºC in orbital shaker at 200 rpm (REMI CIS 24 BL). YPD medium consisted of 2% (w/v) glucose, 2% peptone, and 1% yeast extract (Hi Media, India).

2.2 Synthesis of complex $[CoCu_2(C_{12}H_{33}N_5O_{15}S)]$

An ethanolic solution of cobalt chloride hexahydrate (1 mmol) was added drop wise with constant stirring to ethanolic solution of dimethylglyoxime (2 mmol). The stirring was continued for 30 min. at about 70^0C followed by dropwise addition of (1 mmol) ethanolic solution of diethanolamine. The resulting mixture was refluxed for 3 hrs. The brown reddish mixture was then cooled and an ethanolic solution of $CuCl_2.4H_2O$ (2 mmol) was added. The mixture was further refluxed for 2 hrs. at 50^0C. The hot mixture was then filtered and (1 mmol) aqueous solution of ammonium sulphate was added to it. The filtrate was kept in a $CaCl_2$ desiccator. Dark reddish single crystals suitable for X-ray data collection were obtained from the filtrate after a few days.

Yield: 50%; mol. Wt. 705.49 $gmol^{-1}$; dark reddish crystals; anal. Calc. for $[CoCu_2(C_{12}H_{33}N_5O_{15}S)]$(%): found(calculated): C, 20.20% (20.43%); H, 4.39% (4.43%); N, 9.90% (9.92%); S, 4.50% (4.54%); IR (KBr pellets, cm^{-1}): 1125(N-O), 490(Cu-O, oxime oxygen); ESI-MS (m/z) for $[M-(SO_4+4H_2O+Cl+DEA+2H^+)]$: 410.4. Found: 410.7; λmax. = 815nm.

2.3 Solution Stability

A quantitative estimation of the stability of the complexes at physiological pH was obtained by monitoring their UV-Vis spectra in aqueous solutions of PBS at pH 7.4. Over a period of 24 h. the solutions of the complexes (10^{-4} M) were prepared in aqueous solutions of PBS at pH 7.4. The hydrolysis profiles of the complexes were assessed by recording their electronic spectra over 24 h at 25^oC [25].

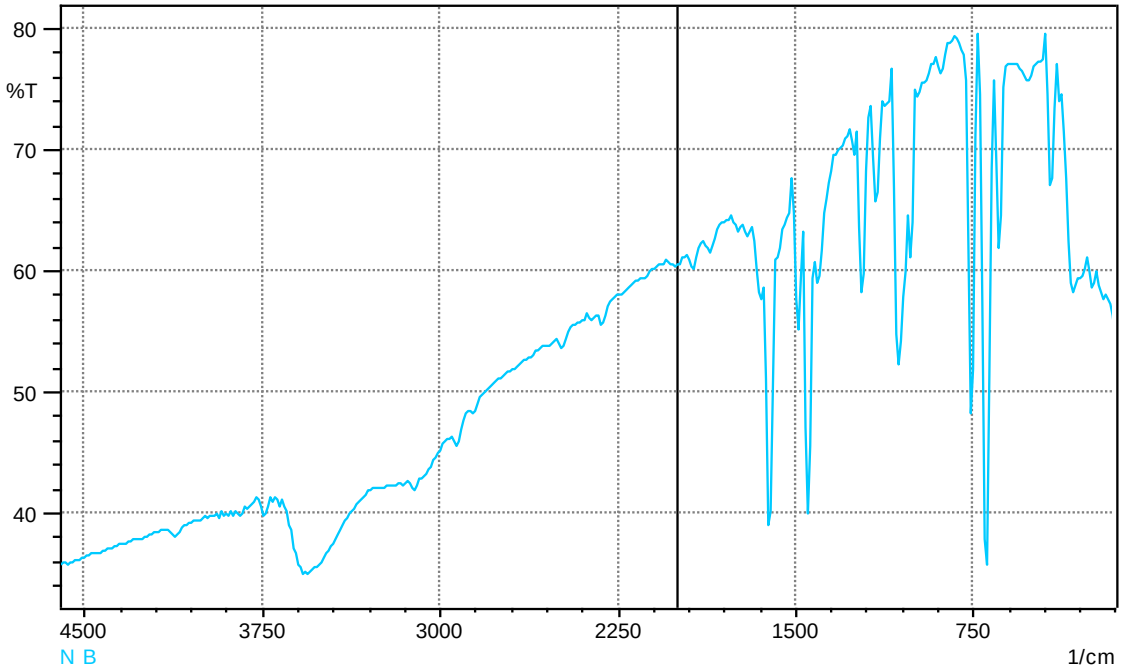


Figure 1: FT-IR of compound

2.4 Biological Screening

2.4.1 Minimal inhibitory concentration (MIC)

The minimal inhibitory concentration (MIC) is the lowest concentration of the test compound that causes inhibition of visible growth (turbidity). MIC_{80} was determined *in vitro* in liquid medium by the broth micro dilution method as per the guidelines of CLSI reference document M27-A3 [26] for fungi. Fluconazole was included as positive control in this study. In addition to this, a drug-free control was also included.

2.4.2 Disk diffusion assay

The assay was performed as discussed previously [27]. Briefly, strains were inoculated into liquid media and grown overnight at 37ºC. Cells were then washed three times with distilled water and approximately 1×10^5 cells/ml were inoculated into half-strength molten agar media at 42ºC and poured into 100 mm diameter petri-plates. After the top layer had solidified; sterile paper discs (4 mm) were impregnated with the test compounds and placed on the agar surface. After incubation at 37ºC for 48 h, the size and pattern of the growth inhibition zone around the disc on agar were evaluated.

3. RESULTS AND DISCUSSION

The coordination complex was synthesized by condensation of deprotonated cobaltdimethylglyoxime containing diethanolamine as axial ligands with copper chloride [scheme 1]. The metal complexes were obtained as dark reddish crystals in good yield (50-55%). The complex was air-stable solid, soluble in water and insoluble in other solvents. The complex was characterized by elemental analysis, IR, ESI-MS, UV-visible spectroscopy and conductivity measurements.

3.1 FT-IR spectrum

FT-IR of the complex was recorded as KBr disc. The medium intensity band in the range of 1010-1020 cm^{-1} due to ν(N-O) and absence of broad peak at about 3400cm^{-1} is consistent with absence of

hydrogen bonded OH and hence presence of deprotonated cobalt oxime. The sharp peak at 490 cm^{-1} indicates coordination of dimethylglyoxamato dianion with copper. Medium to high intensity band at 3150 cm^{-1} is consistent with the presence of water molecules coordinated to terminal copper ions.

3.2 ESI mass spectrum

ESI-MS was recorded in positive ion mode and indicates the evidence of the formation of the binuclear trimetallic coordination complex [Figure 1]. The (M+1) peak was not observed. However many fragments were observed in the spectrum which characterize the composition of complex. The peaks corresponding to fragments with general formula [M-SH_8O_8Cl(DEA)+2H^+)], [M-$SH_8O_{10}Cu$(DEA)] at m/z 410.7 and 255.9 respectively were observed (where DEA=diethanolamine and M=$CoCu_2C_{12}H_{31}N_5O_{14}SCl$). The base peak was observed at m/z 97.4 which corresponds to the fragment [dimethylglyoxime-H_2O].

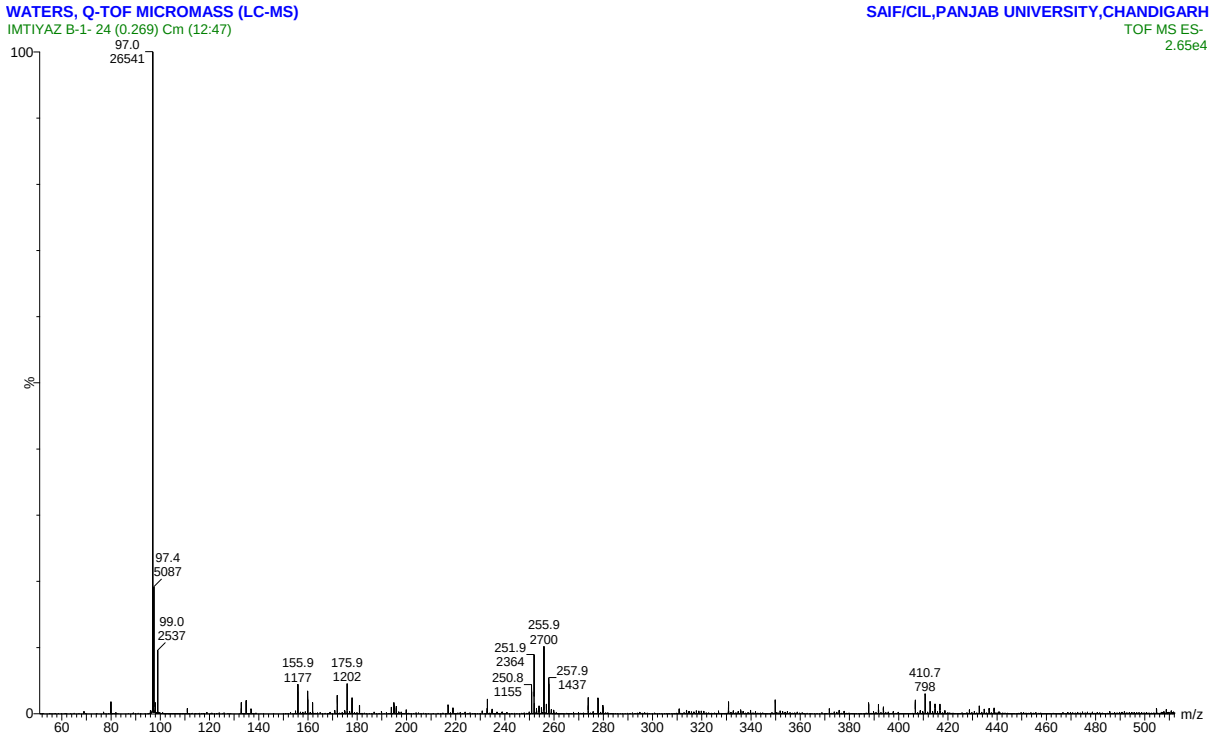


Figure 2: ESI-MS of complex

3.3 Molar conductivity

Molar conductance measurement of the complex was carried out in double distilled water at room temperature. Molar conductance value for 10^{-3} M solution of complex was 87.5 $\Omega^1cm^2M^{-1}$. This value is in accordance with their 1:1 nature [28-30].

3.4 UV-Vis spectrum

UV-Vis of complex in water has been measured in 200-1200 nm range. In addition to the highly intense ligand centered n→σ* transition at 213 nm and π→π* transition at 266 nm, two other broad bands were observed at 850 nm and 1035 nm [Figure 2]. On the basis of low extinction coefficient and relative broadness, the broad maximum at 850 nm and a relatively weak absorption feature at 1035 nm are

assigned to ligand field (d-d) transitions occurring at terminal Cu (II) centers. The energy of these transitions is insensitive to different solvents, hence lending further support to d-d nature of these broad bands. Absorption bands with comparable features have been previously assigned to high spin copper (II) complexes having square pyramidal structure with considerable distortions [31].

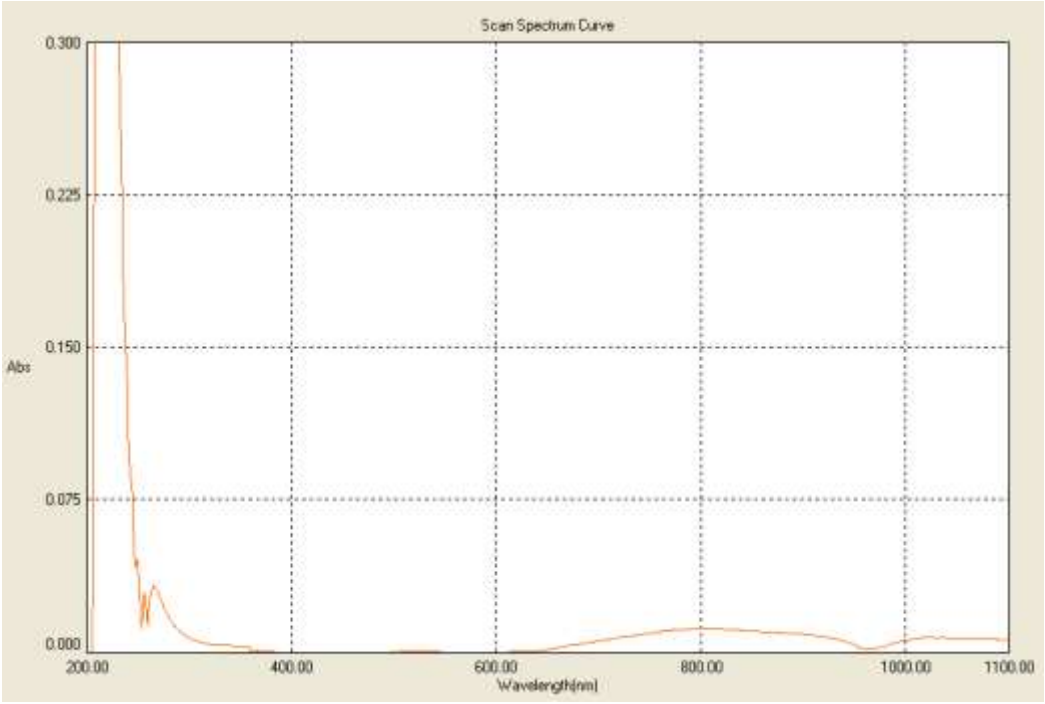


Figure 3: UV-Vis of complex

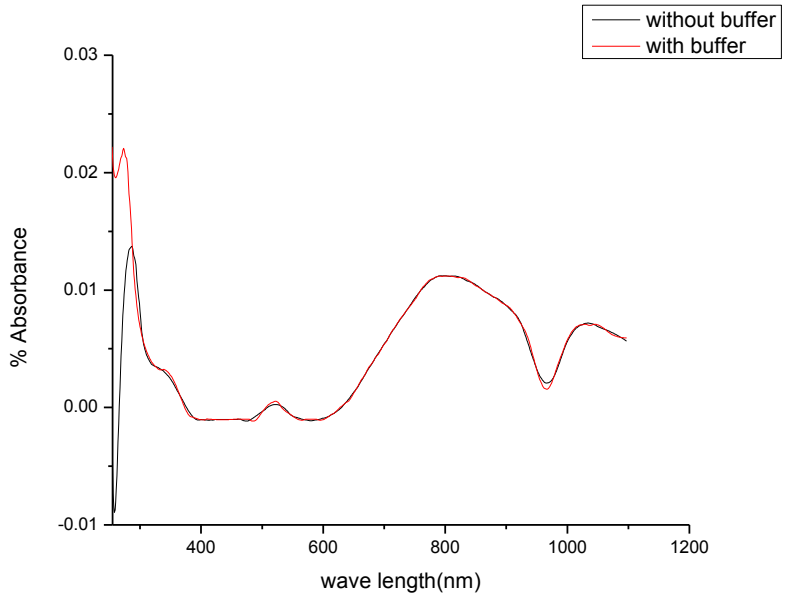


Figure 4: Solution Stability of complex

3.4 Solution stability

Aquation is an important process for the action of a large number of therapeutically active drugs. UV-Vis absorption spectroscopy is often used for the solution stability studies of complex at physiological pH. Complex displayed similar spectra in PBS with no shifts in their bands shown in figure 3 after 24 h and also resisted precipitation over this time period. All these observations indicated the robust nature of the complex [25].

3.5 Cyclic Voltameter

Cyclic Voltameter was carried out using three electrode system and is shown in figure 4. In water with 0.1 M acetic acid, reversible reductions were observed for the $Co^{III/II}$ couple at -0.06 V vs SCE and for the $Co^{II/I}$ couple at -0.38 V vs SCE. Addition of $TsOH.H_2O$ (0.15 mM) to an unstirred solution of (0.1 M) acetic acid in water produced a catalytic wave at a potential close to the position of $E°(Co^{II/I})$ for complex. At low acid concentrations, the catalytic wave had a peak-like shape, but for higher acid concentrations the current approached a plateau at potentials more negative than $E°(Co^{II/I})$. The potential at which catalysis took place remained nearly constant with increasing acid concentration. No catalytic waves were observed at potentials near the $E°(Co^{III/II})$, consistent with the fact that this potential was significantly more positive than the thermodynamic potential for hydrogen evolution using tosic acid as the proton source. Similar behaviour was observed when $HBF_4.Et_2O$ was used as the proton source. Hence, complex is a catalyst for electrochemical H_2 evolution in acidic aqueous solutions and the catalysis is associated with reduction of the Co(II) complex to its Co(I) state.

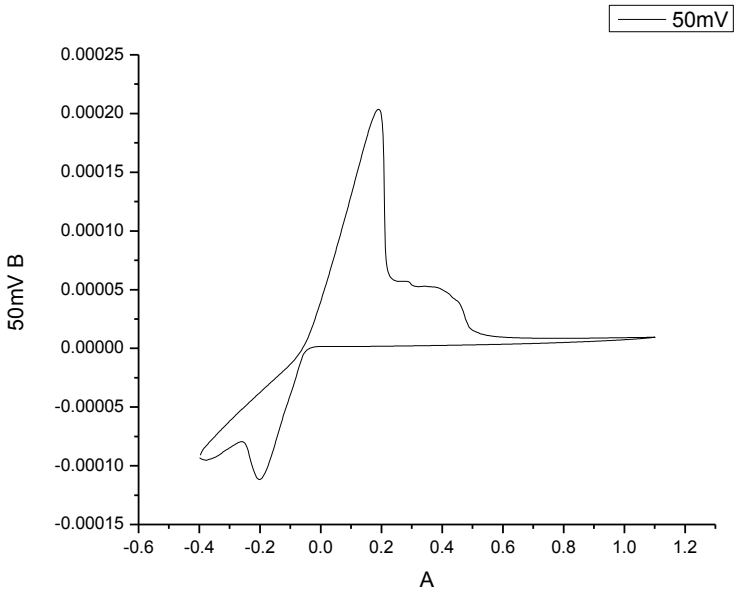


Figure 5: Cyclic Voltameter of complex

3.6 Antifungal Acivity

3.6.1 Minimum Inhibitory Concentration (MIC80)

The Minimum Inhibitory Concentration was defined as the lowest concentration of the complex that causes 80% decrease in absorbance (MIC80) compared with that of the control (no test compound) [Table 1]. The MIC80 of metal complex and standard drugs were determined against *Candida albicans* ATCC 90028 broth dilution method (BDM). The complex has MIC80 160 µg/ml.

Table 1. *In vitro* antimicrobial activity of complex.

Test agents	MIC (µg/ml) *C. albicans* ATCC 90028
B1 Complex	160
Fluconazole (standard drug)	2.5-7.5

Table 2. Disk diffusion assay of *C. albicans* ATCC 90028 showing inhibition in the presence of synthesized complex.

S.No.	Test concentration (µg)	Zone of Inhibition (mm)	
		B1 (Complex)	Fluconazole
1.	200	*	22
2.	400	*	*
3.	1000	8	*
4.	2000	14	*

*no inhibition halo

Figure 6. Disk diffusion assay of *C. albicans* ATCC 90028 showing zones of inhibition in the presence of complex [B1]. The concentration of the test compounds ranged from 200-2000 µg per disk. Fluconazole (FLU) (2.5-7.5 µg) was used as a positive control.

3.6.2 Disc Diffusion Assay

Synthesized compounds were investigated for their antimicrobial activity by agar diffusion method (Table-2). Antifungal activity (*in vitro*) of the complex was studied against *Candida Albicans* ATCC 90028 at the concentration range of 200µg/ml and 2000µg/ml (10 fold more than MIC). At higher concentration the complexe show significant antimicrobial activity against the tested pathogens. Higher concentrations of the complexe was used to get visible results. At higher concentration (2000µg/ml) the highest zone of inhibition *i.e.* 14 mm was measured in *Candida albicans* when treated

complex respectively [figure 5]. The result showed that, in case of solvent control disc no zone of inhibition was observed so as far as our study is concerned 10% DMSO, as a solvent is having no effect on the tested organisms. Results obtained demonstrated that the ability to kill *Candida* species is dependent on the concentration of the test compound. The tested *Candida* isolate used in this study showed high degree of sensitivity for metal complexes as is evident from the large zones of inhibition. Hence we can effectively conclude here that whole of the antifungal effect is due to the different concentration of the metal complex used in this study.

This result is significant as the conventional drug fluconazole is fungistatic and hence leads to antifungal drug resistance. Of course the complexation of the metal ion has brought about enhancement in activity. Our results are also supported by the study which shows that metal ions are thought to reduce polarity and, thereby, allowing effective attachment of complexes with the cell membranes creating pores leading to the loss of essential cell ingredients and consequent cell death [32].

4. CONCLUSION:

The synthesis of heterotrimetallic complex has been described. The complexes were obtained in good yield. The complex may attributed to square planar geometry. The structure of the complex was proposed mainly on the basis of spectroscopic data. The MICs obtained gave a good indication of the overall antifungal effectiveness of each test compound. This indicates that complex displayed anticandidal activities against *Candida ablicans*. Although it was still less active than fluconazole, it can be used as a good starting point for further optimizations. The complex is a catalyst for electrochemical H_2 evolution in acidic aqueous solutions and the catalysis is associated with reduction of the Co(II) complex to its Co(I) state. The future of this field lies in gaining a better understanding of the fundamental transformations occurring at heterobimetallic centers and assessing the independent roles of each metal and/or the polar metal-metal bonds in reactivity.

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REFRENCES

[1] Turner J.A.; Sustainable Hydrogen Production. *Science*, **2004**, *305*, 972-974.

[2] Weast R.C.; Astle M.J.; Beyer W.H.; *CRC Handbook of Chemistry and Physics*, CRC Press: Boca Raton, FL, **1983**, ed. *64*.

[3] Millet P.; Durand R.; Pineri M.; Preparation of new Solid Polymer Electrolyte composites for water electrolysis. *Int. J. Hyd. Energy*, **1990**, *15*, 245-253.

[4] Michas A.; Millet P.; Metal and metal oxides based membrane composites for Solid Polymer Electrolyte water electrolysis. *J. Membr. Sci.*, **1991**, *61*, 157-165.

[5] Millet P. ; Alleau T. ; Durand R. ; Characterization of membrane-electrodes assemblies for Solid Polymer Electrolyte water electrolysis. *J. Appl. Electrochem.*, **1993**, *23*, 322.

[6] Bard A.J.; Inner-sphere heterogeneous electrode reactions. Electrocatalysis and photocatalysis: the challenge. *J. Am. Chem. Soc.*, **2010**, *132*, 7559-7567.

[7] Cook T.R.; Dogutan D.K.; Reece S.Y.; Surendranath Y.; Teets T.S.; Nocera D.G.; Solar Energy Supply and Storage for the Legacy and Non-legacy Worlds. *Chem. Rev.*, **2010**, *110*, 6474-6502.

[8] Li F.; Jiang Y.; Zhang B.; Huang F.; Gao Y.; Sun L.; Nitrogen-Doped graphene foams as metal-free counter electrodes in high-performance DSSCs. *Angew. Chem., Int. Ed.*, **2012**, *51*, 12124-12127.

[9] Concepcion J.J.; Jurss J.W.; Brennaman M.K.; Hoertz P.G.; Patrocinio A.O.v.T. Murakami Iha N.Y.; Templeton J.L.; Meyer T.J.; Making oxygen with ruthenium complexes. *Acc. Chem. Res.*, **2009**, *42*, 1954-1965.

[10] Youngblood W.J.; Lee S.H.A.; Maeda K.; Mallouk T.E.; Visible light water splitting using dye-sensitized oxide semiconductors. *Acc. Chem. Res.*, **2009**, *42*, 1966-1972.

[11] Hambourger M.; Moore G.F.; Kramer D.M.; Gust D.; Moore A.L.; Moore T.A.; Biology and technology for photochemical fuel production. *Chem. Soc. Rev.*, **2009**, *38*, 25-35.

[12] Roeser S.; Farràs P.; Bozoglian F.; Martínez-Belmonte M.; Benet-Buchholz J.; Llobet A.; Chemical, Electrochemical, and Photochemical Catalytic Oxidation of Water to Dioxygen with Mononuclear Ruthenium Complexes. *ChemSusChem*, **2011**, *4*, 197-207.

[13] Xu Y.; Duan L.; Tong L.; Akermark B.; Sun L.; Visible light-driven water oxidation catalyzed by a highly efficient dinuclear ruthenium complex. *Chem. Commun.*, **2010**, *46*, 6506-6508.

[14] Xu Y.; Fischer A.; Duan L.; Tong L.; Gabrielsson E.; Akermark B.; Sun L.; Chemical and Light-Driven Oxidation of Water Catalyzed by an Efficient Dinuclear Ruthenium Complex. *Angew.Chem. Int. Ed.*, **2010**, *49*, 8934-8937.

[15] Eisenberg R.; Gray H.B.; Preface on making oxygen. *Inorg. Chem.*, **2008**, *47*, 1697-1699.

[16] Koelle U.; Transition metal catalyzed proton reduction. *New J. Chem.*, **1992**, *16*, 157–169.

[17] Artero V.; Fontecave M.; Some general principle of designing electrocatalysts with hydrogenase activity. *Coord. Chem. Rev.*, **2005**, *249*, 1518–1535.

[18] Shima S.; Pilak O.; Vogt S.; Schick M.; Stagni M.S.; Meyer- Klaucke W.; Warkentin E.; Thauer R.K.; Ermler U.; The crystal structure of [Fe]-hydrogenase reveals the geometry of the active site. *Science*, **2008**, *321*, 572-575.

[19] Gloaguen F.; Lawrence J.D.; Rauchfuss T.B.; Biomimetic Hydrogen Evolution Catalyzed by an Iron Carbonyl Thiolate. *J. Am. Chem. Soc.*, **2001**, *123*, 9476-9477.

[20] Dempsey J.L.; Brunschwig B.S.; Winkler J.R.; Gray H.B.; Hydrogen evolution catalyzed by cobaloximes. *Acc. Chem. Res.*, **2009**, *42*, 1995-2004.

[21] Wilson A.D.; Newell R.H.; McNevin M.J.; Muckerman J.T.; DuBois M.R.; DuBois D.L.; Hydrogen oxidation and production using nickel-based molecular catalysts with positioned proton relays. *J. Am. Chem. Soc.*, **2006**, *128*, 358-366.

[22] Nguyen M.T.D.; Charlot M.F.; Aukauloo A.; Structural, Electronic, and Theoretical Description of a Series of Cobalt Clathrochelate Complexes in the Co(III), Co(II) and Co(I) Oxidation States . *J. Phys. Chem. A.*, **2011**, *115*, 911-922.

[23] DuBois M.R.; Du Bois D.L.; Development of Molecular Electrocatalysts for CO_2Reduction and H_2 Production/Oxidation. *Acc. Chem. Res.*, **2009**, *42*, 1974-1982.

[24] Voloshin Y.Z.; Varzatskii O.A.; Novikov V.V.; Strizhakova N.G.; Vorontsov I.I.; Vologzhanina A.V.; Lyssenko K.A.; Romanenko G.V.; Fedin M.V.; Ovcharenko V.I.; Bubnov Y.N.; Tris-dioximate cobalt(I, II, and III) clathrochelates: stabilization of different oxidation and spin states of an encapsulated metal ion by ribbed functionalization. *Eur. J. Inorg. Chem.*, **2010**, 5401.

[25] Wani W.A.; Al-Othman Z.; Ali I.; Saleem k.; Hsieh M.F.; Copper(II), nickel(II), and ruthenium(III) complexes of an oxopyrrolidine-based heterocyclic ligand as anticancer agents. *J. coord. Chem.*, **2014**, *12*, 2110-2130.

[26] Wayne, P.A. *Clinical and laboratory standards institute*, 3rd edition, vol. 28, **2008**, M27-A3.

[27] Ahmad A.; Khan A.; Manzoor N.; Khan L.A.; Evolution of ergosterol biosynthesis inhibitors as fungicidal against Candida. *Microb Pathog.*, **2010**, *48*, 35-41.

[28] Shukla S.N.; Gaury P.; Mehrotray R.; Prasad M.; Kaury H.; Prasady M.; Srivastava R.S.; Tailored synthesis, spectroscopic, catalytic, and antibacterial studies of dinuclear ruthenium (II/III) chloro sulfoxide complexes with 5-nitro-ophenanthroline as a spacer. *J. Coord. Chem.*, **2009**, *62*, 2556–2568.

[29] Fry F.H.; Fallon G.D.; Spiccia L.; Zinc(II) complexes of xylyl bridged bis(1,4,7-triazacyclononane) derivatives. *Inorg. Chim. Act.*, **2003**, *346*, 57-66.

[30] Imran A.; Waseem W.;Kishwar S.; Empirical Formulae to Molecular Structures of Metal Complexes by Molar Conductance. *Metal-Organic, and Nano-Metal Chemistry*, **2013**, *43*, 1162-1170.

[31] (a) Adhikary B.; Lucas C.R.; Synthesis, characterization of Cu (II) complexes of N_2S_3 ligand involving aromatic nitrogen and thioether donor. *Inorg. Chem.*, **1994**, *33*, 1376-1381. (b) Bianchi A.; Garcia-Espana E.; Micheloni M.; Nardi N.; Vizza F.; Synthesis of the new thia-aza cage 12,17-dimethyl-5-thia-1,9,12,17-tetraazabicyclo[7.5.5]nonadecane. Thermodynamic studies on protonation and copper(II) complex formation. *Inorg. Chem*. **1986**, *25*, 4379-4381. (c) Hathaway B.J.; *In ComprehensiVe Coordination Chemistry*; Wilkinson G.; Gillard R.D.; McCleverty J.A.; Eds.; Pergamon Press: Oxford, England, **1987**, 5, 533.

[32] Chohan Z.H.; Pervez H.; Khan K.M.; Rauf A.; Maharvi G.M.; Supuran C.T.; Antifungal cobalt(II), copper(II), nickel(II) and zinc(II) complexes of furanyl-,thiophenyl-, pyrrolyl-, salicylyl- and pyridyl-derived cephalexins. *J Enzym Inhib Med Chem.*, **2004**, *19*, 85-90.

The authors declare no conflict of interest

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