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Research Article

DNA CLEAVAGE AND ANTIMICROBIAL ACTIVITY STUDIES OF MANGANESE (II) COMPLEXES CONTAINING 4'-(THIOPHEN-2-YL)-2,2':6',2''-TERPYRIDINE

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A B S T R A C T

Mononuclear manganese(II) complexes having NNN-donor 4'-(1H-thiophen-2-yl)-2,2':6',2"-terpyridine base has been prepared and characterized by various physico-chemical techniques. Manganese(II) complexes show strong ligand to metal charge transfer (LMCT) band in the region of 340-350 nm. Agarose gel electrophoresis method has been employed to study the DNA cleavage behavior of the complexes. The synthesized ligands and complexes have been tested for in vitro growth inhibitory activity against two Gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis), two Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa), and two fungi (Aspergillus niger and Candida albicans). Both the ligand and complexes exhibit better antimicrobial activities. But the antimicrobial activity of the complexes has been found to be higher due to its chelating nature.

INTRODUCTION

Organisms require multiple life sustaining processes such as metabolic pathways for conversion of food to energy, transport pathways to remove unwanted byproducts, and reproductive mechanisms to generate new cells. Metals are receiving ever-increasing recognition for their roles in biological processes. Manganese is the 12th most abundant element and 3rd most abundant transition metal. It is well known that manganese plays a vital role in many biological systems including photosystem-II (water oxidation), catalase (disproportion of the hydrogenperoxide) and superoxide dismutase (dismutation of superoxide radical) [1]. The coordination chemistry of nitrogen donor ligands is an active and interesting area of research. Organic compounds containing pyridine rings play significant roles in many biological reactions [2]. Also many transition and heavy metal cations play active roles in several biological processes. Polypyridines are becoming increasingly important in many areas [3]. Several hundred metal polypyridine complexes have been prepared and used over the past few decades [4]. Much of the interest in these compounds stem from their possible applications. A range of 6, 6"-disubstituted derivatives of 2, 2': 6',2" - terpyridine have been prepared by Edwin C. Constable and Jack Lewis [5] with the intention of forming macro-cycles incorporating the 2,2':6',2"-terpyridyl moiety.

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A high yield route to 6, 6"- bis (methylhydrazino - 4'- phenyl - 2, 2': 6', 2"- terpyridine is described. A number of complexes of this pentadentate ligand have been prepared with metal salts of Cr^{III}, Mn^{II}, Fe^{II}, Co^{II} and Ni^{II} and characterized. Torsten Wieprecht *et al* [6] have studied terpyridine - manganese complexes as a new class of bleach catalysts for detergent applications. These complexes were investigated with respect to their physico - chemical properties and bleach performance. It is found that introduction of electron - donating hydroxy and amine substituents at the 4-position of the individual pyridine rings improves the bleach performance in model experiments conducted at 40 and 25°C at pH 10. Four saccharinate complexes of divalent transition metals with 2, 2': 6', 2"-terpyridine as co - ligand have been synthesized by Robert M.K. Deng *et al* [7]. The complexes [M (tpy)(sac)$(H_2O)_2$] (where M = Mn, Co, Ni and sac = sugar) which are structural have been characterized by elemental analysis and X-ray crystallography.

Monika Walesa - Chorab *et al* [8] have synthesized mononuclear complexes of the dimethyl terpyridine (L) of the general formula MLX_2 where M = Mn^{II}, X = Cl, Br, NO_3, ClO_4 and M= Zn^{II}, X = Cl, NO_3. The complexes were characterized through analytical, spectroscopic (UV-vis, ESI - MS and IR) and magnetic measurements. Single crystal X - ray structure analysis of these complexes revealed five-coordination of metal ions. Zohreh Naseri *et al* [9] have investigated the first row transition metal complexes of a thienyl substituted terpyridine. The metal complexes $[M(thiotpy)_m(X)_n]$ where thiotpy = 4'-(2-thienyl)- 2, 2': 6',2"-

terpyridine, X = NO_3^-/OAc^- and M = Cr^{III}, Mn^{II}, Fe^{II}, Co^{II}, Ni^{II} and Cu^{II} have been characterized using elemental analysis, IR and electronic spectra (UV-vis, fluorescence). Crystallographic studies were carried out on the Cr^{III} nitrate and Cu^{II} acetate complexes. The biological activity studies indicate that the complexes show excellent antibacterial, antineoplastic and remarkable superoxide scavenging properties. Four complexes of 4'-phenyl - 2,2':6',2"- terpyridine (L) formulated as $[Cu(L)Cl_2].2H_2O$ (**1**); $[Cu\ (L)\ Cl_2].CH_3OH$ (**2**); $[(L)Cl\ Mn\ (\mu\text{-}Cl)_2\ MnCl\ (L)]$. $2[Mn\ (L)Cl_2].2CH_3OH$ (**3**) and $[Fe\ (L)_2]\ (FeCl_4).CH_3OH$ (**4**) were synthesized by Ting-Hong Huang *et al* [10]. Noemie Elgrishi *et al* [11] have synthesized and characterized terpyridine complexes of first row transition metals (bivalent Mn, Fe, Co, Ni, Cu and Zn) having compositions $[M\ (tpy)_2]\ X_2$, where X = ClO_4^{--} or PF_6^- and evaluated them as catalysts for the electrocatalytic reduction of CO_2 to CO. To assess the reactivity of M - tpy complexes towards CO_2 at reducing potentials, cyclic voltammetry experiments were carried out in DMF / H_2O (95:5 v: v) solutions of each complex under air and CO_2 saturated conditions. A terpyridine ligand 4'-(2-ferrocenyl)-2,2':6,2"-terpyridine (fctpy) was reacted with divalent metal ions (Cu,Co,Mn, Ni and Zn) by Annu Juneja *et al* [12] to get complexes of general formula $[M(fctpy)_2](PF_6)_2$. The complexes were characterized by various spectroscopic techniques to suggest an octahedral geometry around the central metal ion. These complexes were screened for their antiamoebic, trypanocidal and antimalarial activities. 4'-Chloro-2, 2': 6', 2''-terpyridine (Cltpy) is a well known and commercially available member in the tpy family whose coordination chemistry has been extensively investigated since it was initially introduced in 1990. Both mono and bis – ligand transition metal complexes $M(Cltpy)X_2$ and $M(Cltpy)_2X_2$, where M = Mn^{II}, $Fe^{II,}$ Ni^{II}, Zn^{II}, Cd^{II} or Ru^{II} have been reported. The synthesis, structures and catalytic properties of novel Cu^{II} and mixed valent Cu^{I}, Cu^{II} complexes of Cltpy with a focus on their structure – activity relationship in catalysis have also been reported by E.C.Constable *et al* [13].

In view of these fascinating properties and applications of metal complexes of derivatives of 2, 2':6',2''- terpyridine, we ventured to synthesize and characterize 4'- substituted terpyridine 4'-(thiophen- 2 - yl)- 2, 2':6',2'' - terpyridine, and its coordination compounds with bivalent manganese perchlorate. We also ventured to study the biological properties (anti–microbial and DNA cleavage activities) of the newly synthesized compounds.

Experimental Section

MATERIALS AND METHODS

2-acetyl pyridine, manganese (II) perchlorate, agarose (molecular biology grade) and ethidium bromide were procured from Sigma Aldrich, USA and used as received. Other materials like sodium hydroxide, ammonium acetate and solvents like methanol, acetonitrile were of reagent grade. The ligand, stpy (thiophenyl terpyridine) was prepared using published procedure [14]. Buffers were prepared using deionised and sonicated triple distilled water. Tris (hydroxymethyl) aminomethane–HCl (Tris–HCl) buffer (pH, 7.2) was used for DNA cleavage studies. UV–visible spectra of the complexes were recorded on a Perkin–Elmer Lambda 35 double beam spectrophotometer at 25°C. IR spectra were recorded as KBr pellets in the 400 - 4000 cm^{-1} region using a Shimadzu FT–IR 8000 spectrophotometer. Positive ion electron ionization mass spectra of the complexes were obtained by using Thermo Finnigan LCQ 6000 advantage max ion trap mass spectrometer. All the DNA gel images were taken using UVITEC gel documentation system and fragments were analysed using UVIchem and UVI-band software.

Synthesis of Ligand

Synthesis of 4'-(thiophen-2-yl)-2,2':6',2''-terpyridine (stpy) (L1)

4'-(Thiophen-2-yl)-2,2':6',2"-terpyridine was prepared by adapting the procedure available in the literature. 2-Acetylpyridine (1.12 mL, 10 mmol) and 1*H*-thiophen-2-carboxaldehyde (0.48 g, 5 mmol) were combined using a mortar and pestle. The grinding was continued until an orange red powder formed (within 10 minutes). The powder was added to a suspension of ammonium acetate (2.5 g) in glacial acetic acid (10 mL) and heated to reflux for 2 hours. The crude product was precipitated out by the addition of water (5 mL). The product was filtered, washed with water and cold ethanol and it was recrystallised to get white powder. Yield: 1.29 g, 82 %, Analysis Calculated for $C_{19}H_{13}N_3S$: C, 72.38; H, 4.13; N, 13.33 %; Found: C, 72.34; H, 4.11; N, 13.30 %. EI-MS: m/z 316.19 $(M+1)^+$; IR, cm^{-1}(KBr pellet) 3054, 1610, 1565, 1266. UV-Visible λ_{max}, nm: 285, 321.

Synthesis of Manganese (Ii) Complexes

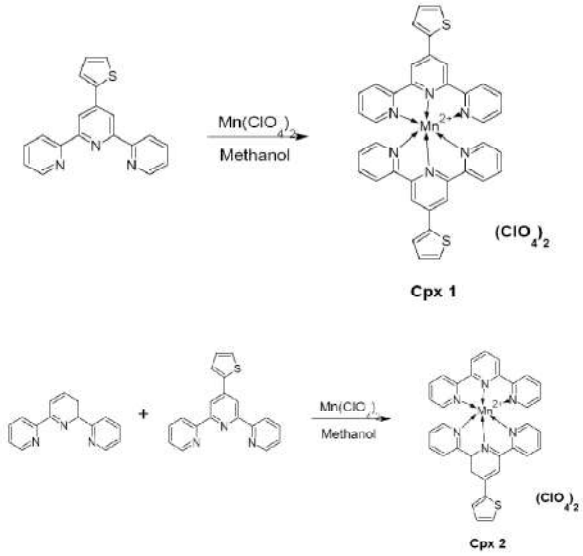

Figure 1 Synthetic scheme for Manganese (II) Complexes

Synthesis of $[Mn(stpy)_2](ClO_4)_2$ (1)

Caution! During handling of the perchlorate salts of metal complexes with organic ligands, care should be taken because of the possibility of explosion.

The ligand thiophenyl terpyridine (stpy) was prepared by slight modification of the reported procedure. The compound was prepared in high yield. To a hot solution of $Mn(ClO_4)_2.\ 6H_2O$ (0.5 g, 1.3 mmol) in methanol, stpy (0.94 g, 2.6 mmol) dissolved in was added slowly and the reaction mixture was refluxed for 15 minutes. A white solid that separated out upon

slow evaporation of the solvent, was filtered and washed with diethyl ether. Yield: 0.89 g (78 %). Analysis Calculated for $C_{38}H_{26}MnN_6S_2O_8Cl_2$: C, 51.52; H, 2.94; N, 9.49; Mn, 6.21 %. Found: C, 51.48; H, 2.91; N, 9.46; Mn, 6.19 %. EI-MS: m/z 885.51 $(M+1)^+$; IR, cm^{-1}(KBr pellet) 3061, 1616, 1558, 1249, 1087. UV-Visible λ_{max}, nm: 295, 335.

Synthesis of [Mn(stpy)(tpy)](ClO$_4$)$_2$ (2)

To a hot solution of $Mn(ClO_4)_2$. $6H_2O$ (0.5 g, 1.3 mmol) in methanol, stpy (0.94 g, 1.3 mmol) and tpy (0.94 g, 1.3 mmol) dissolved in methanol was added slowly and the reaction mixture was refluxed for 15 minutes. A white solid that separated out upon slow evaporation of the solvent, was filtered and washed with diethyl ether. Yield: 0.88 g (84 %). Analysis Calculated for $C_{34}H_{24}MnN_6SO_8Cl_2$: C, 50.77; H, 2.98; N, 10.45; Mn, 6.85 %. Found: C, 50.72; H, 2.95; N, 10.42; Mn, 6.81 %. EI-MS: m/z 803.52 $(M+1)^+$; IR, cm^{-1}(KBr pellet) 3074, 1610, 1503, 1242, 1090. UV-Visible λ_{max}, nm: 292, 350.

Experimental Methods of Biological Studies

DNA Cleavage Experiment

A. Preparation of 0.8 % (w/v) Agarose gel

0.8 % Agarose gel (100 mL) was prepared by adding 0.8 g of agarose gel powder and 100 mL of TBE buffer in a 500 mL Schott bottle. The mixture was then heated and stirred evenly by using hot plate stirrer, until all of the agarose gel powder was completely dissolved in the TBE buffer (pH 7.2). Subsequently, 100 µL of 1 M ethidium bromide was added into it. Then, the mixture was poured into the gel mould (Thermo) with comb and allowed to solidify at room temperature.

Agarose Gel Electrophoresis

The cleavage of plasmid DNA, pUC 19 by manganese metal complexes was monitored using agarose gel electrophoresis technique. The experiments were carried out using SC pUC19 DNA under aerobic conditions. Samples were prepared in dark at 25°C by taking 3 µL of SC DNA and 6 µL of the complex from a stock solution in DMSO followed by dilution in 10 mM Tris-HCl buffer (pH 7.2) to make the total volume 25 µL. Chemical nuclease experiments were carried out under dark conditions for one hour incubation at 37°C in the absence and presence of an activating agent H_2O_2 and monitored using agarose gel electrophoresis. Supercoiled pUC19 plasmid DNA in 5 mM Tris-HCl buffer at pH 7.2 was treated with each of the manganese(II) complexes. The samples were incubated for 1 h at 37°C. The reactions were quenched by using loading buffer (0.25 % bromophenol blue, 40 % (w/v) sucrose and 0.5 M EDTA) and then loaded on 0.8 % agarose gel containing 0.5 mg/mL ethidium bromide. Another set of experiment was also performed using DMSO and histidine in order to find out the type of reactive species involved in the cleavage mechanism. The gels were run at 50 V for 3 h in Tris-boric acid-ethylenediamine tetra acetic acid (TBE) buffer and the bands were photographed by a UVITEC gel documentation system.

Antimicrobial Assay

Micro-Organisms used

Four species of bacteria, two gram positive (*Staphylococcus aureus & Bacillus subtilis*) and two gram negative (*Escherichia coli & Pseudomonas aeruginosa*) and two fungi (*Candida albicans & Aspergillus niger)* were obtained from KMCH, Coimbatore and employed for *in vitro* antimicrobial screening of test compounds.

Preparation of Inoculum

A loopful of strain was inoculated in 30 mL of nutrient broth in a conical flask and incubated on a rotary shaker at 37°C for 24 hours to activate the strain.

Bioassay

The bioassay used was the standard Agar disc diffusion assay. Mueller Hinton Agar was prepared for the study. Mueller Hinton agar plates were swabbed with a suspension of each bacterial species, using a sterile cotton swab. Subsequently, the sterilized filter paper discs were completely saturated with the test compounds. The impregnated dried discs were placed on the surface of each inoculated plate. The plates were incubated overnight at 37°C. Each compound was tested against each organism in triplicate. Methanol was used as negative control. Standard discs of Gentamycin and Clotrimazole served as positive antibacterial control. The test materials having antimicrobial activity inhibited the growth of the micro-organisms and a clear, distinct zone of inhibition was visualized surrounding the disc. The antimicrobial activity of the test agents was determined by measuring the diameter of zone of inhibition in mm.

RESULTS AND DISCUSSION

Synthesis and Spectral Characterization

The tridentate thiophenyl terpyridine ligand (stpy) was prepared according to a known procedure reported already and characterized. The manganese(II) complexes with formula $[Mn(stpy)_2](ClO_4)_2$ (1) and $[Mn(stpy)(tpy)](ClO_4)_2$ (2) where stpy is the tridentate ligand 4'-(thiophenyl-2,2':6',2''-terpyridine and tpy is 2,2':6',2''-terpyridine has been isolated from methanolic solution containing manganese(II) perchlorate as the starting material. Both the complexes were obtained in good yield and characterized by using EI-MS, electrical conductance, elemental analysis, UV-Vis, IR and emission spectral techniques. The synthetic scheme of the present complexes is shown in Figure 1. The positive ion electron ionization mass spectra of the manganese(II) complexes 1 and 2 showed a major peak at 885.51and 803.52 respectively. The analytical and mass spectral data are consistent with the proposed formula of the manganese(II) complexes. Based on electrical conductance measurement, manganese(II) complexes is proposed to be 1:2 electrolytes as they measure molar conductance at 148.0 Scm^2mol^{-1} and 153 Scm^2mol^{-1} respectively in $\sim 10^{-3}$ M DMF solution. The electronic spectra of both the ligand and complexes in acetonitrile solution showed two bands each in the region of 227-285 nm and a broad band in the 350 nm region for complexes alone. The electronic spectra of 1 and 2 showed two types of transitions, the first one appeared at range 227-285 nm which could be assigned to π-π* and n-π* transitions due to transitions involving molecular orbitals located on the ligands. From the spectra it has been observed that both the complexes exhibited broad ligand to metal charge transfer transition in the region of 335-350 nm. The infrared spectra of the ligand and its complexes are recorded in KBr medium. The C-H stretching vibrational frequencies of thiophenyl terpyridine are observed at 3054-3074 cm^{-1}. The pyridine ring skeletal vibrations (C=C

and C=N) appear at 1546 – 1436 cm^{-1}. The C–H out-of-plane bending vibrations appear at 786 and 731 cm^{-1}. The pyridine ring in-plane deformation is observed at 621 cm^{-1} whereas the out-of-plane ring deformation is found at 480 cm^{-1}. In the spectrum of complex **1**, absorptions in the region 1610-1565 cm^{-1} are attributed to the C=C and C=N ring stretching frequencies of the terpyridyl ligand. Presence of peak at 1087 cm^{-1} confirms the presence of perchlorate in complex 1. These vibrations have not shown appreciable shifting due to coordination but the in-plane ring deformation vibration of the pyridyl ligands have shifted to a higher value of 623 cm^{-1} indicating the coordination of the terpyridyl ligand in complex 1. The very strong absorption found at 1090 cm^{-1} is attributed to the presence of ionic perchlorate in the complex 2. All the synthesized compounds are able to emit light in the region of when they are excited at the wavelength of 332-368 nm. When compound 1 is excited at 340 nm, it emits light at the wavelength of 411 nm. Similarly compound 2 and ligand L1 exhibit emission at 545and 451 nm respectively.

DNA Cleavage Studies of Manganese (II) Complexes

The characterization of DNA recognition by transition metal complex has been aided by the DNA cleavage chemistry that is associated with redox-active or photo-activated metal complexes [15]. Many manganese complexes have been shown to cleave DNA in the presence of H_2O_2 due to their ability to behave like a Fenton catalyst. The ability of present complexes to effect DNA cleavage was monitored by gel electrophoresis using supercoiled pUC19 DNA in Tris-HCl buffer.

Control experiments suggested that untreated DNA and DNA incubated with complex 1 or 2 or peroxide alone did not show any significant DNA cleavage. However, interestingly in the presence of hydrogen peroxide, both the complexes 1 and 2 were found to exhibit nuclease activity. The cleavage behavior of both the complexes is shown in figures 2 and 3. As shown in Figure 2, at a higher concentration of 100 µM, the complexes showed complete cleavage. It is believed that when the present redox active manganese complexes were interacted with DNA in the presence of hydrogen peroxide as an oxidant hydroxyl radicals might be produced [16-19]. These hydroxyl radicals are responsible for cleavage of DNA. In order to establish the reactive species responsible for the cleavage of DNA, experiment in the presence of histidine and DMSO were carried out. On adding the standard hydroxyl radical scavenger DMSO to the reaction mixture of the complex and DNA, the DNA cleavage activity of 1 and 2 decreased significantly. Interestingly, addition of histidine did not affect the cleavage activity of 1 or 2. This suggested that singlet oxygen species were not involved in this reaction. This conclusively shows the involvement of the hydroxyl radical in the observed nuclease activity of complexes 1 and 2 in the presence of peroxide.

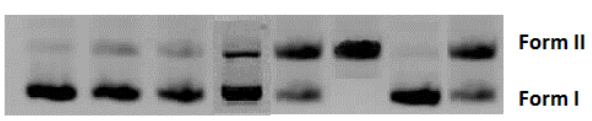

Figure 2 Cleavage of pUC19 DNA by Complex 1

DNA was incubated with complex for 60 min in Tris buffer (pH 7.2) at 37°C. Lane 1, DNA control; lane 2, DNA + peroxide (100 µM); lane 3, DNA + 1 (24 µM) alone; lane 4, DNA + 1(24 µM) + peroxide (100 µM); lane 5, DNA + 1 (60 µM) + peroxide (100 µM); lane 6, DNA + 1 (100 µM) + peroxide (100 µM); lane 7, DNA + 1 (100 µM) + peroxide (100 µM) + DMSO (10 mM); lane 8, DNA + 1(100 µM) + peroxide (100 µM) + Histidine (10 mM).

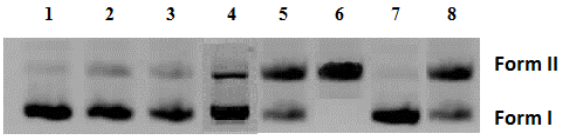

Figure 3 Cleavage of pUC19 DNA by Complex 2

DNA was incubated with complex for 60 min in Tris buffer (pH 7.2) at 37°C. Lane 1, DNA control; lane 2, DNA + peroxide (100 µM); lane 3, DNA + 2 (24 µM) alone; lane 4, DNA + 2 (24 µM) + peroxide (100 µM); lane 5, DNA + 2 (60 µM) + peroxide (100 µM); lane 6, DNA + 2(100 µM) + peroxide (100 µM); lane 7, DNA + 2 (100 µM) + peroxide (100 µM) + DMSO (10 mM); lane 8, DNA + 2 (100 µM) + peroxide (100 µM) + Histidine (10 mM).

Antimicrobial Activity

The antimicrobial activities of both the ligand (L1) and its manganese (II) complexes were studied by agar well diffusion method and the results were shown in Tables 1 and 2. *In vitro* antimicrobial activity of a test drug is measured in terms of zone of inhibition produced. Higher the diameter of zone higher is the microbial growth inhibition. It is observed that the growth inhibition activities of the test compounds increase with increase of concentrations of test compounds. A comparison of the activities of the ligand and its complex against *S.aureus* shows the order: 2 > 1 > L1. It is to be noted that these compounds exhibit greater activity than the standard Gentamycin.

Comparing the antibacterial activities of test drugs against *B.subtilis* shows the order : 2 > 1 ~ L1. In the case of *E.coli* the activities decrease in the order: 2 > 1> L1. When the test drugs are assayed against *P.aeruginosa,* it is observed that compound 1 display greater activity. Thus it is seen that the compounds tested are sensitive to the bacteria used, and all the compounds tested are much more active than the standard antibacterial drug namely gentamycin. The antifungal activity results furnished in Table 2 indicate that the test drugs show enhanced activity against the test fungi (*A.niger and C.albicans*) when the concentrations of drugs are increased. Also the test drugs are less sensitive against the fungi compared to the standard drug viz. clotrimazole. The activities of test drugs against *A.niger* decrease in the order: 1 > 2> L1. The sensitivities of test drugs to *C.albicans* are found to decrease in the order : 1 > 2 > L1. The newly synthesized compounds showed zone of inhibition ranging from 10 to 25 mm. The comparative studies of the ligand and its manganese(II) complexes signify that the complex showed significantly enhanced antimicrobial activity against microbial strains in comparison to the free ligands. The enhanced antimicrobial activity of the complexes can be explained by Tweedy's chelation theory and overtone's concept. According to the Overtone's concept of cell permeability, the lipid membrane surrounding the cell favors the passage of only lipid-soluble materials;

Table 1 Antibacterial Activity of Ligand and its Manganese (II) Complexes

S.No.	Test Drug	Zone of Inhibition (mm)															
		S. aureus				*B. Subtilis*				*E. coli*				*P. aeruginosa*			
		25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL
1	Stpy (L1)	12	14	18	20	10	12	14	16	16	18	20	19	12	14	17	18
2	$[Mn(stpy)_2](ClO_4)_2$ (**1**)	14	16	16	22	12	13	15	16	16	18	20	22	14	16	18	23
3	$[Mn(tpy)(stpy)](ClO_4)_2$ (**2**)	18	20	22	25	14	16	18	20	18	14	16	24	12	14	16	20
4	Gentamycin Standard	-	-		18	-	-		20	-	-	-	20	-	-	-	25

Note: Zone size less than 15 mm – Least active; 16 – 20 mm– moderatively active; Above 20 mm – highly active

therefore, liposolubility is an important factor which controls the antimicrobial activity. On chelation, polarity of the metal ion is reduced to a greater extent due the overlapping of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Moreover, delocalization of the π-electrons over the whole chelate ring is increased, and lipophilicity of the complexes is enhanced. The increased lipophilicity enhances the penetration of the complexes into the lipid membranes and blocks the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism. In general, metal complexes are more active than ligands as they may serve as principal cytotoxic species.

Table 2 Antifungal Activity of Ligand and its Manganese (II) Complexes

S.No	Test Drug	Zone of Inhibition (mm)							
		A. niger				*C. albicans*			
		25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL
1	Stpy (L1)	16	18	20	17	10	12	14	16
2	$[Mn(stpy)_2](ClO_4)_2$ (**1**)	10	12	15	22	18	20	23	25
3	$[Mn(tpy)(stpy)](ClO_4)_2$ (**2**)	14	16	18	20	14	16	19	22
4	Clotrimazole Standard	-	-		20	-	-	-	25

Note: Zone size less than 15 mm – Least active; 16 – 20 mm– moderatively active; Above 20 mm – highly active

CONCLUSIONS

We have prepared two manganese(II) complexes 1 and 2 having 4'-(thiophenyl)-2,2':6',2"-terpyridine ligand with a metal to heterocyclic base ratio as 1:2 and 1:1 respectively. Both the complexes were characterized by various physico-chemical techniques and a six coordinated distorted octahedral environment has been proposed for the complex 1 and 2. DNA cleavage was brought about by the manganese complexes in the presence of hydrogen peroxide. The involvement of hydroxyl radical in the oxidative cleavage reactions is evidenced from the inhibition reactions in presence of DMSO. And also the complexes are able to show better activity against the microbes than that of the ligand.

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References

1. Pecoraro, VL., Baldwin, MJ., Gelasco, A. 1994. Interaction of manganese with dioxygen and its reduced derivatives. Chem. Rev., 94*:* 807-826.
2. Baldwin, MJ., Kampf, JW., Kirk, ML., Pecoraro, VL. 1995. Structural and magnetic studies of Mn(II) complexes of the imidazole-containing ligand 5-NO_2-salimh [5-NO_2-salimh = 4-(2-(5-nitrosalicylideneamino)ethyl)imidazole] with varying nuclearity. Inorg. Chem., 34: 5252-5260.
3. Sauer, K., Yachandar, VK., Britt, RD., Klien, MP. 1992. In Manganese Redox Enzymes; Pecoraro, VL. Ed., VCH, New York.
4. Cargill Thompson AM. 1997. The synthesis of 2,2′:6′,2″-terpyridine ligands — versatile building blocks for supramolecular chemistry. Coord. Chem. Rev., 160: 1-52.
5. Rojo, T., Garcia, A., Mesa, JL. 1989. Copper(II) complexes with 2,2′: 6′,2″-terpyridine. Crystal structure of the dimeric compound $[Cu\ (terpy)(NCO)_2]_2 \cdot 2H_2O$. Polyhedron, 8: 97-102.
6. Hathcock, DJ., Stone, K., Madden, J., Slattery, SJ. 1998. Electron donating substituent effects on redox and spin state properties of iron(II) bis-terpyridyl complexes. Inorg. Chim. Acta., 282: 131-135.
7. Liu, X., McInnes, EJL., Kilner, CA., Pett, MT., Halcrow, MA. 2001. Metal complexes of 4′-(3-phenylpropoxy)-2,2′:6′,2″-terpyridine and 4′-(3-propoxy)-2,2′:6′,2″-terpyridine. Polyhedron, 20: 2889-2900.
8. Harriman, A., Mayeux, A., Nicola, AD., Ziessel, R. 2002. Synthesis and photophysical properties of ruthenium (II) *bis* (2,2′:6′,2″-terpyridine) complexes constructed from a diethynylated-thiophene residue. Phys. Chem. Chem. Phys., 4: 2229-2235.
9. Rakhimov, RD., Weinstein, YA., Lileeva, EV., Zheligovskaya, NN., Melnikov, MYa., Butin, KP. 2003. Electrochemical properties of 2,2":6",2″-terpyridine complexes of platinum(II) with arenethiolate ligands. Alkylation of reduced forms of the complexes Russian. Chem. Bulletin., 52: 1150-1156.
10. Hong Huang, T., Zhang, M., Gao, C., Wang, L. 2013. Synthesis, structures and characterization of metal complexes containing 4′-phenyl-2,2′:6′,2″-terpyridine ligands with extended π···π interactions. J. Inorg.Chim.Acta., 408: 91-95.

11. Billings, SB., Mock, MT., Wiacek, K., Turner, MB., Kassel, WS., Takeuchi, KJ., Rheingold, AL., Boyko, WJ., Bessel, CA. 2003. Comparison of (triphenylphosphine) ruthenium complexes containing the 2,2′:6′,2″-terpyridine (trpy) and 4,4′,4″-tri-*t*-butyl-2,2′:6′,2″-terpyridine (trpy*) ligands. Inorg. Chim. Acta., 355: 103-115.
12. Juneja, A., Soares Macedo, T., RodrigoD., Moreira, M., Botelho Pereira Soares, M., Cristina Lima Leite, A., Kalle de Andrade T., Neves, L., Rego Alves Pereira, V., Avecilla, F., Azam, A. 2014. Synthesis of 4′-(2-ferrocenyl)-2,2′:6′2″-terpyridine: Characterization and antiprotozoal activity of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes. Eur. J. Med. Chem., 75: 203-210.
13. Hammam, AM., Ibrahim, SA., El – Gahami, MA., Fouad, D. 2003. Investigations of Co(II), Ni(II) and Cu(II) (2,2´:6´,2"2"-terpyridine) complexes with sulfur donor ligands. J. Therm. Anal. Cal., 74: 801-810.
14. Kröhnke, F. 1976. The specific synthesis of pyridines and oligopyridines. Synthesis, 1: 1-24.
15. Berg, JM., Lippard, SJ. 2004. Bioinorganic chemistry. Curr. Opin. Chem. Biol., 8: 160-161.
16. Thyagarajan, S., Murthy, NN., Narducci-Sarjeant, AA., Karlin, KD., Rokita, SE. 2006. Selective DNA strand scission with binuclear copper complexes: implications for an active $Cu_2{-}O_2$ species. J. Am. Chem. Soc., 128: 7003-7008.
17. Pyle, AM., Barton, JK. 1990. Probing nucleic acids with transition metal complexes. Prog. Inorg. Chem., 38: 413-475.
18. Morrow, JR., Iranzo, O. 2004. Synthetic metallonucleases for RNA cleavage. Curr. Opin. Chem. Biol., 8: 192-200.
19. Perrin, DM., Mazumder, A., Sigman, DS. 1996. In Progress in Nucleic Acid Chemistry and Molecular Biology, Cohnk W, Moldave ed.; Academic Press: New York Orlando, 52: 123-129.

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