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SYNTHESIS, COMPOSITION, GEOMETRY AND ANTIBACTERIAL ASSAY OF MONONUCLEAR SCHIFF BASE METAL COMPLEX DERIVED FROM 1H-INDOLE-2, 3-DIONE AND ANILINE

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ABSTRACT

Mononuclear Schiff base metal complex of Mn(II) and its ligand have been synthesized with Schiff base derived from 1H-Indole-2, 3-dione and aniline. The structure of the ligand and its complex were characterized through physico-chemical studies. The molar conductance value of metal complex in DMF indicates the non-electrolytic in nature. In IR spectra, the comparison of shift in frequency of the complex with the ligand reveals the coordination of donor atoms to the metal atom. The d-d transition of the metal complex provides information about the geometry of the complex and the transitions are in good agreement for the proposed octahedral geometry. The Schiff base and its complex have been screened for their *in vitro* antibacterial (*staphylococcus aureus, bacillus subtilis, Eschericia coli and Klebsilla pneumonia*) activity by paper disc method, it result confirms the mononuclear complex is more potent than free ligand.

KEYWORDS: *Staphylococcus aureus, bacillus subtilis, Eschericia coli and Klebsilla pneumonia.*

INTRODUCTION

The designing and synthesis of a new ligand was perhaps the most important step in the development of metal complexes which exhibit unique properties and novel reactivity due to electron donor, electron acceptor properties, structural, functional groups and the position of the ligand in the coordination sphere. This may be the factor for different studies[1-2]. A large number of Schiff base compounds are often used as ligands in coordination chemistry by considering their metal binding ability. Schiff bases have gained importance because of physiological and pharmacological activities associated with them. Schiff base metal complexes have ability to reversibly bind oxygen in epoxidation reactions[3], biological activity[4-5], catalytic activity in hydrogenation of olefins[6-7] nonlinear optical materials[8] and photochromic properties[9]. The Schiff base complexes was also used as drugs and they possess a wide variety of antimicrobial activity against bacteria, fungi and it also inhibits the growth of certain type of tumors[10-13].

In view of these finding, this piece of work has devoted with the aim to synthesize transition metals complex with Schiff bases ligand from 1H-Indole-2, 3-dione and aniline and to examine their physical properties involving spectral behaviours, the electrical conductance values and to determine the efficiency of the synthesized complex against pathogenic bacteria.

MATERIALS AND METHODS

All the chemicals were purchased from commercial sources and used without any further purification.

Analytical and physical measurements

C, H and N analyses were carried out using a Perkin-Elmer 2400-II elemental analyzer. FT-IR data were recorded as KBr disc using Thermo Nicolet, Avatar 370 model spectrometer in the range 4000-400 cm^{-1}. UV-Vis spectra were obtained in DMF on a Perkin-Elmer Lambda 40(UV-Vis) spectrometer in the range 200-800 nm. Molar conductance of the complex in DMF was measured using an Elico model conductivity meter. Magnetic susceptibility measurements were carried out by employing the Gouy method at room temperature. NMR signals were obtained from Bruker Avance III, 400MHz model spectrometer.

Synthesis of Schiff base

The Schiff base ligand was synthesized by adding 1H-Indole-2, 3-dione (1 mM) in 20 ml of ethanol, and aniline (2 mM) in 20 ml of ethanol. The mixture was refluxed for 2 1/2 hrs. Then solution of the ligand was kept for slow evaporation and coloured precipitate was collected and dried in air.

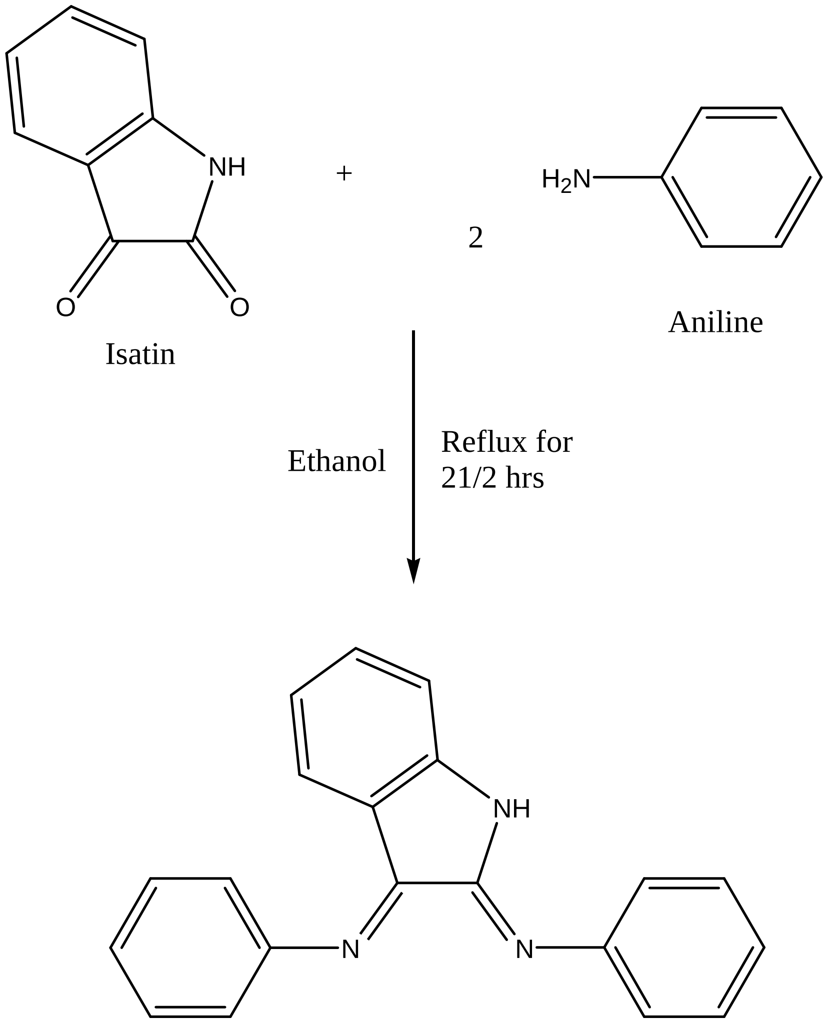

Fig 1. Synthesis of Schiff base ligand

Synthesis of Mononuclear Schiff base Metal complex

The ethanolic solution of synthesized ligand (2mM) was added dropwise stirring to an ethanolic solution of the metal salt (1 mM) with constant stirring, and the mixture was boiled under reflux for 41/2 hrs. Then, the volume of the reaction mixture was reduced by evaporation. The precipitated complex were filtered off, washed with ethanol and then dried in *vacuuo*.

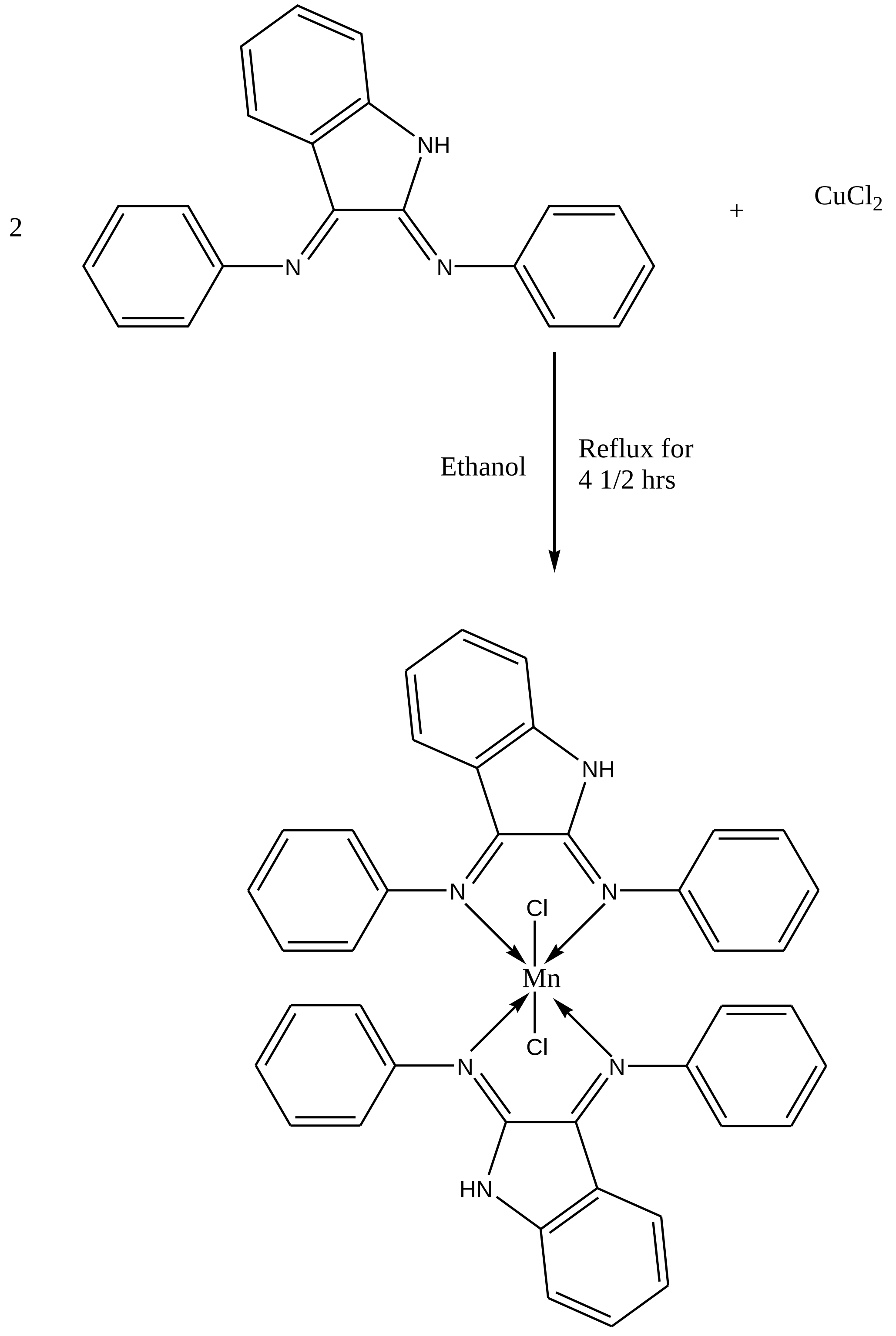

Fig 2. Synthesis of Mn(II) Schiff base metal complex

Antibacterial assay

The standard disc diffusion method was followed to determine the antibacterial activity of the synthesized compounds against the sensitive organism *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Klebsilla pneumonia*[14]. The tested compounds were dissolved in

DMF (Which have no inhibition activity). The disc of Whatmann no.4 filter paper having the diameter 8.00 mm were soaked in the solution of compounds in DMF. Uniform size filter paper disks were impregnated by equal volume from the specific concentration of dissolved tested compounds and carefully placed on incubated agar surface. After incubation for 36 hrs at 27^0 C in the case of *bacteria*, inhibition of the organism which evidenced by clear zone surround each disk was measured and used to calculate mean of inhibition zones.

DNA cleavage experiments

For the gel electrophoresis experiments, supercoiled pUC18 DNA was treated with synthesized complex in Tris buffer (50 µM H_2O_2 in Tris-HCl buffer pH 7.2), and the solution was irradiated at room temperature with a UV lamp (365 nm, 10 W). After being incubated at 37 °C for 2 hrs, electrophoresis was carried out at 50 V for 2 h in Tris–acetic acid- EDTA buffer. Electrophoresis was carried out and bands were visualised by UV light and photographed to determine the extent of DNA cleavage from the intensities of the bands[15].

RESULTS AND DISCUSSION

Analytical data of the Schiff base ligand and its mononuclear metal complex are given in Table.1. and are in well agreement with the expected values. The synthesized Mn(II) complex is colored, non hygroscopic solids, stable in air. They are sparingly soluble in ethanol, acetone and chloroform and completely soluble in DMF and DMSO.

Table 1. Analytical data of the Schiff base ligand and its mononuclear metal complex

Compound	Molecular Formula	Colour	Yield %	Melting Point (°)	% of Nitrogen		% of Metal	
					Cal	Exp	Cal	Exp
L	$C_{20}H_{15}N_3$	Yellow	70	200	14.14	14.12	-	-
MnL_2X_2	$Mn(C_{40}H_{30}N_6Cl_2)$	Dark green	65	290	10.88	10.86	12.44	12.42

Molar conductivity measurements

The molar conductance value of the synthesized complex was determined using 10^{-3}M concentration in DMF as solvent, are in the range of 7.50 Ω^{-1} cm^2 mol^{-1}. This value suggests non-electrolyte nature for Mn ($C_{40}H_{30}N_6Cl_2$) complex.

Table 2. Molar conductance data of the Schiff base complex

Compounds	Solvent	Molar conductance $ohm^{-1}cm^{2}mol^{-1}$	Type of electrolyte
Mn ($C_{40}H_{30}N_6Cl_2$)	DMF	7.50	Non electrolyte

IR Spectra

The FT-IR spectral analysis of complex indicated the presence of all expected functionalities is listed in Table 3 and 4. This compound exhibited the absorptions of azomethine region at lower frequencies than free ligand. The infrared spectrum of the Schiff base ligand showed a medium absorption at 1613.67 cm^{-1} assinged to the C=N stretching vibrations, indicating the formation of the Schiff base linkage. In the complex, this band is shifted to lower frequencies in the 1612.95 cm^{-1}upon complexation with the metal[16], which can be attributed to the coordination of the imine nitrogen to the metal centre. The characteristic bands for the entire complex in the region 689.94 cm^{-1} may assigned for the vibration of aromatic rings and C-H stretching respectively. The other absorption characteristic appeared in the region 470.51 and 312.06 cm^{-1} may be assigned for M-N and M-Cl vibrations[17].

Table 3. IR data of ligand

Group	Expected υ cm^{-1}	Observed υ cm^{-1}
Aromatic C-H stretching	3100-3000	3070.12
Aromatic C=C skeleton	1600-1500	1591.27
C-H in plane bending of phenyl group	1100-1000	1055.91
C-H out of plane bending of phenyl group	900-650	689.94
C=N stretching	1690-1470	1613.67
N-H stretching	3000-3400	3162.40

Table 4. IR data of Schiff base metal complex

Compounds	ν (C=N) (cm^{-1})	ν (M-Cl) (cm^{-1})	(M−N) (cm^{-1})
$C_{20}H_{15}N_3$	1613.67	--	--
Mn ($C_{40}H_{30}N_6Cl_2$)	1612.95	312.06	470.51

Electronic spectra and magnetic moment

The electronic absorption spectra of the Mn(II) complex were recorded in freshly prepared solution in DMF at room temperature. The electronic spectra of the Schiff base ligand and their complex have been measured in DMF solution 200– 800 nm at room temperature[18]. In the electronic spectra of the Schiff base ligand, an intense absorption at 324 nm were assigned to a benzene $\pi\rightarrow\pi^*$ transition and the band at 379 nm were assigned due to $n\rightarrow\pi^*$

transition associated with the azomethine chromophore (-C=N). The electronic spectra of Mn(II) complex exhibit two very low intense bands, band at 558 nm which may rise due to $^{6}A_{1g} \rightarrow ^{4}A_{1g}(G)$ transition and the another band at 536 nm may be assigned to $^{6}A_{1g} \rightarrow ^{4}A_{1g}$, 4Eg,(G) transition for Mn(II) ion in octahedral environment[19]. The room temperature magnetic moment of Mn(II) complex 5.62 B.M. is close to the spin only value for an octahedral Mn(II) ion corresponding to five unpaired electrons.

Table 5. Electronic Spectral data of Schiff base ligand and its Mn(II) complex.

Compound	Electronic spectra (nm)				Geometry of the complex
	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$	L→M	d-d	
$C_{20}H_{15}N_3$	324	379	-	-	-
$Mn(C_{40}H_{30}N_6Cl_2)$	292	317	429	558, 536	Octahedral

^{1}H – NMR spectra

The ^{1}H NMR Schiff base was recorded in DMSO-d_6 at room temperature. Three different type of protons were identified

i) the multiplets around 6.4-7.6 ppm are assigned to aromatic protons,

ii) the azomethine group in the Schiff base appears 8.29 ppm was observed and

iii) the N-H protons appear at 11.00 ppm [20].

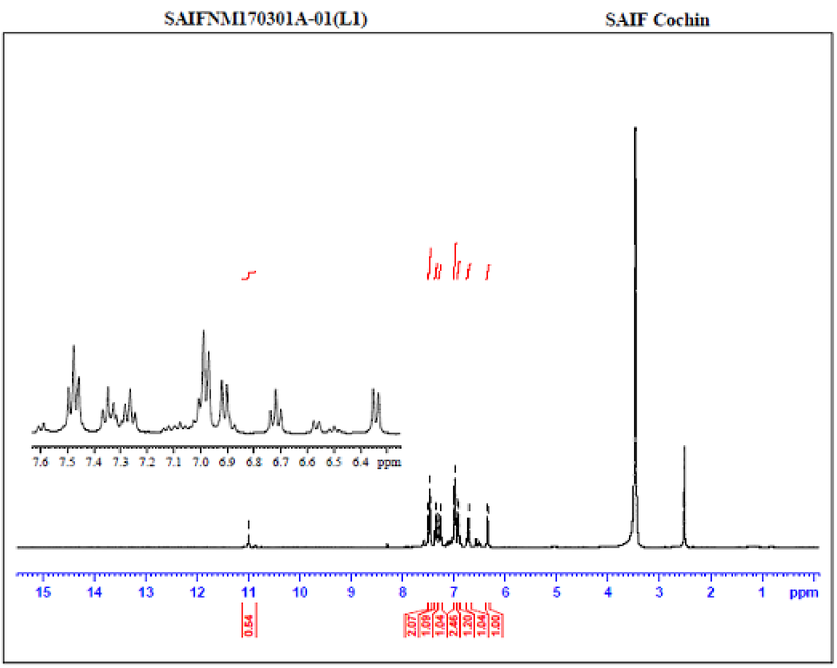

Fig 3. ^{1}H NMR spectrum of $C_{20}H_{15}N_3$

Antibacterial activity

Biological activity of the ligand and its Mn(II) complex were screened for anti-bacterial activity against two gram positive pathogenic strains such as *Staphylococcus aureus, Bacillus subtilis* while *Escherichia coli* and *Klebsilla pneumonia* species were gram negative by disc-agar diffusion method. The ligand shows less effective towards bacteria. Also, it was noted that the complex showed greater inhibition than the ligands. It was evident that overall potency of the ligand was enhanced on coordination with the metal ions. Furthermore, the mode of action of the compound may involve the formation of a hydrogen bond through the azomethine group with the active centre of the cell, resulting in interference with the normal cell process, and the metal complex are generally more active than the ligand[21].

Table 6. Antibacterial activity for Schiff base ligand and its mononuclear metal complex

Compounds	Zone of inhibition (mm)															
	Gram positive bacteria								Gram negative bacteria							
	Staphylococcus aureus				*Bacillus subtilis*				*Escherichia coli*				*Klebsiella pneumoniae*			
	Concentration (µg/mL)															
	25	50	75	100	25	50	75	100	25	50	75	100	25	50	75	100
$C_{20}H_{15}N_3$	7	7	8	9	7	7	9	9	6	6	7	8	7	8	8	9
$Mn(C_{40}H_{30}N_6Cl_2)$	9	8	10	12	9	8	11	12	6	7	7	9	9	8	9	10
Streptomycin	16	17	20	22	14	15	17	20	12	13	16	20	13	14	16	18

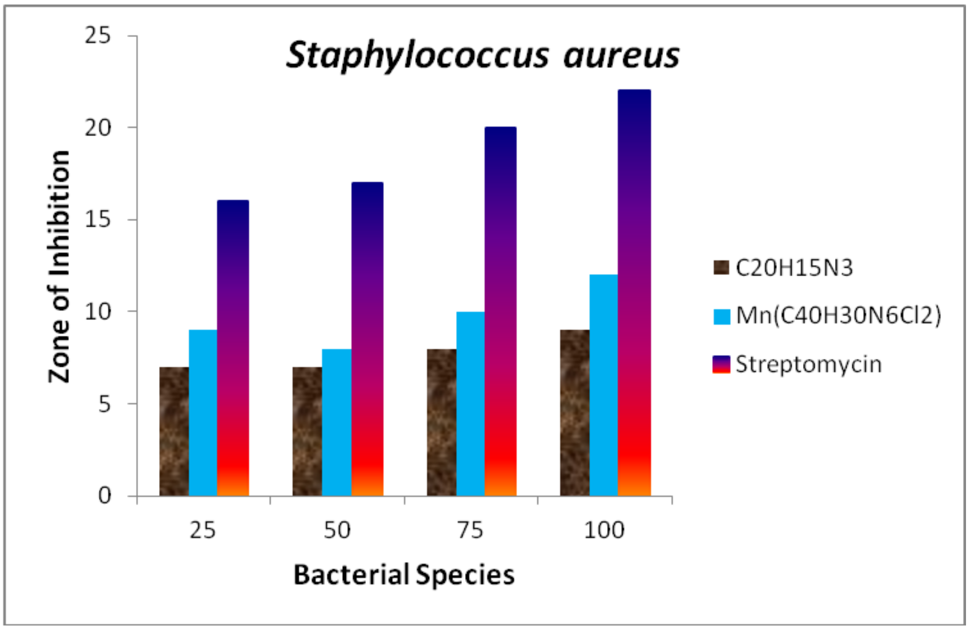

Fig 4. Antibacterial activity of Schiff base ligand and its mononuclear Schiff base metal complex against *Staphylococcus aureus*

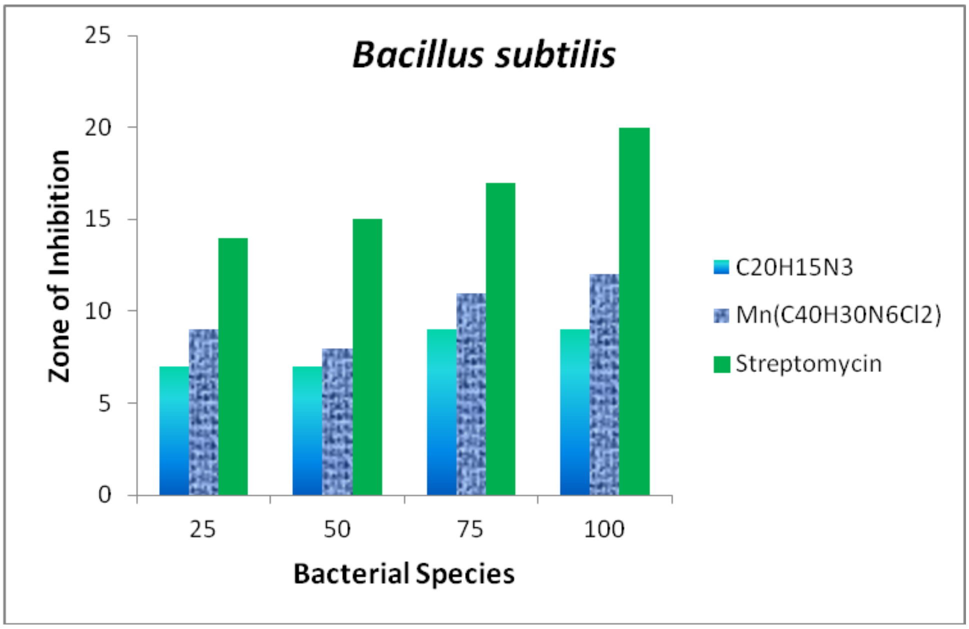

Fig 5. Antibacterial activity of Schiff base ligand and its mononuclear Schiff base metal complex against *Bacillus subtilis*

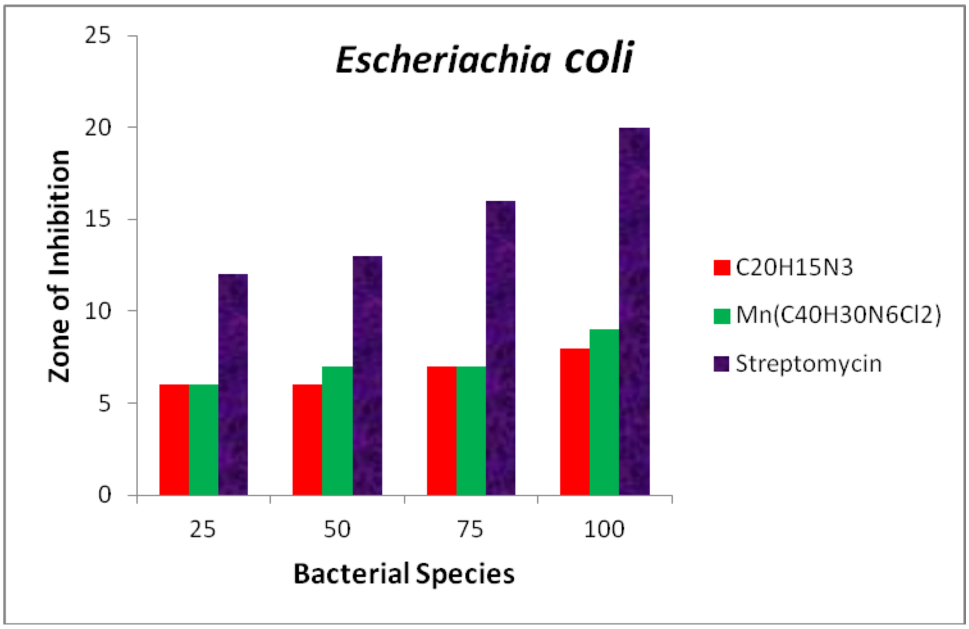

Fig 6. Antibacterial activity of Schiff base ligand and its mononuclear Schiff base metal complex against *Escherichia coli*

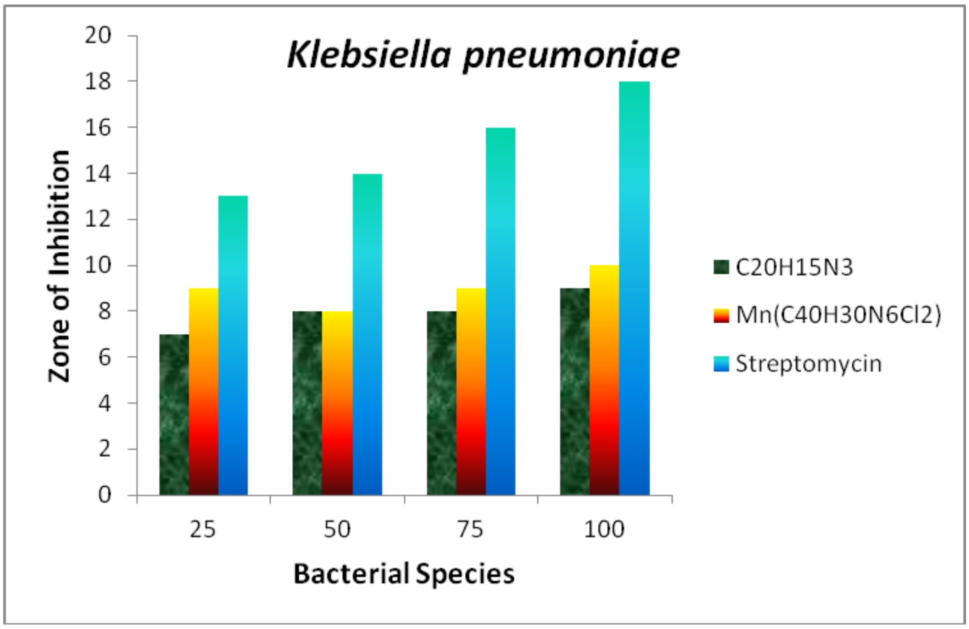

Fig 7. Antibacterial activity of Schiff base ligand and its mononuclear Schiff base metal complex against *Klebsiella pneumonia*

DNA cleavage studies by gel electrophoresis method

More appropriately both the naturally occurring DNA cleavage agents and man-made compounds that can specifically recognize and cut DNA have been termed as chemical nucleases[22]. The DNA cleavage studies was performed with gel electrophoresis method. Gel electrophoresis experiments were performed using pUC18- DNA with ligand, complex in presence of H_2O_2. Complex exhibits cleavage ability at low concentration. The ligand exhibits no significant activity in the presence of oxidant when compared to complex. When DNA is subjected to electrophoresis, relatively fast migration will be observed for the intact super coil form (Form I). If scission occurs on one strand (nicking), the super coil will relax to generate a slower moving open circular form (Form II). If both strands are cleaved, a linear form (Form III) that migrates between Forms-I and -II will be generated[23]. From the figure (20) the complex shows more activity in the presence of oxidant which may due to reaction of hydroxyl radical with DNA.

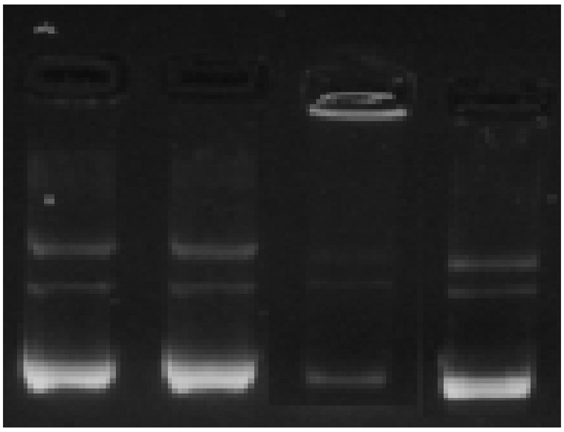

Fig 8. Changes in the agarose gel electrophoretic pattern of pUC18DNA induced by H_2O_2 and metal complex. Lane 1-DNA alone; Lane 2- DNA alone + H_2O_2; Lane 3-DNA + $C_{20}H_{15}N_3$ + H_2O_2; Lane 4-DNA + $Mn(C_{40}H_{30}N_6Cl_2)$ + H_2O_2.

CONCLUSIONS

In this paper, we have explored the synthesis and coordination chemistry of some mononuclear complex derived from 1H-Indole-2, 3-dione and aniline. The ligand behaves as a dibasic hexadentate species upon complexation with the involvement of phenolic oxygen and the nitrogen atoms in coordination for the complex. The newly synthesized Schiff base and its metal complex have been confirmed by the analytical data, IR, UV-Visible, ^{1}H NMR, ESR spectral data, molar conductance and magnetic moment, studies. The antibacterial activity results shows that all complexes have been found to be more potent than its ligand due to the process of chelation dominantly affects the overall biological behavior of the complexes. The DNA cleavage studies revealed that the metal complexes showed good efficiency towards DNA cleavage. Based on the analytical and spectral studies, we propose octahedral geometry to the synthesized complex.

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