IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Complexes of Mn (II) and Fe (III) with Schiff bases Derived from Trimethoprim with Salicyldehyde and Benzaldehyde as Potential Antimicrobial Agents

Dr. Sudhir Kumar Mishra,

Principal, S.S. College, Jehanabad,

Abstract

Complexes of Mn(II) and Fe(III) with trimethoprim Schiff base ligands,HL1 and HL2 derived from salicyldehyde and benzaldehyde were synthesized and investigated. The complexes have been characterized using metal analysis, molar conductance, FT-IR, UV-Vis and melting point, Infrared studies have shown that Mn(II) and Fe(III) ions coordinated to the ligands through azomethine nitrogen of the pyrimidine in all the complexes. The ability of these complexes to inhibit the growth of pathogenic microorganism such as: *Staplococcus pyogenes*, *Bacillus subtilis* (as Gram positive bacteria), *Corynaebacterium specie*, *Shigella dysentriae* (as Gram negative bacteria) and *Candida albicans* (as Fungus species) were compared with the parent drug (trimethoprim).The results of antimicrobial activity have revealed that the complexes are more potent as compared to the parent drug. The MIC and MBC results further confirmed that Fe(III) complexes posses enhanced inhibition against both Gram positive and Gram negative isolates.

Keywords: Coordination, Schiff base, Antimicrobial and Trimethoprim.

Introduction

Coordination chemistry deals with metals and ligands where metals are known to have preferences for certain ligating atoms and adopt specific geometries. The synthesis of new organic ligands is a key approach for the construction of metal–organic complexes with desired structures. Schiff bases have played an important role in the development of coordination chemistry because of their numerous biological applications.

Schiff bases are a class of compounds having azomethine linkage (C=N) and they are widely used in the field of coordination chemistry due to their ability to form stable complexes. They are among the most expedient and versatile ligands which are easily synthesized in a one step classical condensation reaction

through common aldehydes with amines or ketones usually in quantitative yields. Schiff base ligands of heterocyclic compounds and their transition metal complexes are of great interest as simple structural models of biological system due to the presence of hetro atoms such nitrogen, oxygen and sulphur groups. Schiff base ligands have great tendency toward formation of complexes with almost all the transition metal ions. These compounds exhibit wide range of pharmacological activities, such as antiviral, anticancer, antibacterial, antifungal, anticonvulsant and anti-inflammatory activities that can be well illustrated by the large number of drugs in the market containing their functional group. The wide ranges of applications of these compounds have continued to attract interest among inorganic chemists. Many of them are also thermally stable and have synthetic flexibility. Some of these compounds are found to be useful both as clinical diagnostic agents and in chemotherapeutic application. In view of the properties mentioned above, a large number of Schiff bases have been synthesized and extensively studied. The design and synthesis of organic–inorganic hybrid complexes based on strong coordinate bonds and multiple weak non-covalent forces has become a rapidly growing field of research.

The magnitude of the problem worldwide and the impact of Antimicrobial Resistance (AMR) on human health, and on costs for the health-care sector and the wider societal impact, are still largely unknown (WHO, 2014). The rapid emergence of resistant bacteria is occurring worldwide, endangering the efficacy of antibiotics, which have transformed medicine and saved millions of lives. Many decades after the first patients were treated with antibiotics; bacterial infections have again become a threat. The antibiotic resistance crisis has been attributed to the overuse and misuse of these medications, as well as a lack of new drug development by the pharmaceutical industry due to reduced economic incentives and challenging regulatory requirements. Development of antimicrobial drugs was celebrated as one of the great medical triumph story of the twentieth century. Currently, resistance against antimicrobial agents has become public health concern worldwide. Recently, World Health organization (WHO) has issued a statement of great concern regarding bacterial resistance which is becoming a global problem. Trimethoprim (TMP), is an antibiotic widely used for the treatment of infection caused by aerobic bacterial species . The mechanism of action of trimethoprim involves binding to the bacteria DNA, thus hindering multiplicity of the microorganism and subsequently reduce the development of resistance.. In the quest for novel drugs against microbial resistant diseases, the use of metal complexes has received overwhelming attention. This paper presents some Mn(II) and Fe(III) complexes with Schiff bases derived from trimethoprim with salicyldehyde and benzaldehyde and their antimicrobial activities.

Materials and Methods

Chemicals and instruments

All reagents were purchased and all were of Analytical grade (AR) and were used without further purification. Metal analysis was done by EDTA titration. Melting point was determined with the Gallenkamp melting point apparatus. Molar conductivity measurement (10-3 M solutions in methanol) was obtained on the

DDS-307 conductivity meter. The infrared (IR) spectra were recorded in the range of 4000-500 cm^{-1} as KBr disc on Shimadzu FTIR - 8400 S Fourier Transform Infrared Spectrophotometer. Electronic spectra (10^{-3} M) of the ligands and their complexes were measured in methanol in the wavelength range of 200-700 nm.

Synthesis of Schiff base ligands

The Schiff base ligands were prepared using a literature method. This was done by condensation of the salicyldehyde and benzaldehyde respectively with Trimethoprim as amine in 1:1 mole ratio using methanol as solvent.

Synthesis of the complexes

The metal salts , $MnCl_26H_2O$ (0.396g, 0.002mol), $FeCl_36H_2O$ (0.541g, 0.002mol), were added to the solution of the ligands in 1:2 mole ratio (metal-ligand) with continuous stirring until the complex compound was formed. The coloured product was separated by filtration, washed with distilled water and methanol, and dried under vacuum in a desiccator containing calcium chloride.

Antibacterial test

The standard drug Trimethoprim, metal complexes and their ligands were screened against different strains of pathogenic organisms using a modified filter paper disc agar diffusion method described by. The test was conducted in triplicate and the results presented as MEAN ± SEM.

Statistical Analysis

The data obtained for antimicrobial studies were analyzed using one way ANOVA. The results were recorded as MEAN±SEM on Graph Pad in Stat, 2000.

Table 1 : Physical Characteristics of the Legands and their Metal Complexes

Compound	Molecular formula (Molar mass)	Color	Melting points (°C)	Yield (%)	Molar Conductivity ($Scrn^2rno1^{-1}$)	%Metal Found (calc.)
HL^1	$[C_{21}H_{22}N_4O_4]$ (394.44)	Yellow	240-242	73	-	-
HL^2	$[C_{21}H_{22}N_4O_3]$ (370.46)	White	232-235	72	-	-
$[Mn(HL^1)_2Cl_2]$	$[Mn\ (C_{21}H_{22}N_4O_4)_2Cl_2]$	Brown	258-260	87	0.18	5.69 (6.00)
$[Mn(HL^2)_2Cl_2]$	$[Mn(C_{21}H_{22}N_4O_3)_2Cl_2]$	Dark brown	255-258	89	0.11	6.31 (6.34)
$[Fe(HL^1)_2Cl_2]Cl$	$[Fe(C_{21}H_{22}N_4O_4)_2C1_2]Cl$	Brown	275-278	78	0.20	5.50 (5.87)
$[Fe(HL^2)_2Cl_2]Cl$	$[Fe(C_{21}H_{22}N_4O_3)_2Cl_2]Cl$ 903.22	Yellow Ocher	283-285	77	0.28	5.92 (6.18

Table 2: Relevant Infrared Spectral data of the Ligands and their Metal Complexes (cm^{-1})

Compound	u (N112)	u (C=N)	u (C-N)	u (M-0)	u (M-N) iv (M-CI)
HL^1	3462br	1637m	1440sh	-	-
HL^2	3406br	1643m	1481m	-	-
$[Mn(HL^1)_2Cl_2]$	3398s	1656sh	1500sh	439sh	516s
$[Mn(HL^2)_2Cl_2]$	3402s	1643sh	1496m	-	524s
$[Fe(HL^1)_2Cl_2]Cl$	3402vs	1651m	1496m	466w	497sh
$[Fe(HL^2)_2Cl_2]Cl$	3402vs	1654s	1496m	-	489s

br=broad, w=weak, sh=sharp, s= strong, m=medium, vs= very strong

Table 3: Electronic Absorption Spectral data of the Ligands and their Complexes

Compound	$\lambda_{max}(nm)$	Wave number (cm^{-1})	Band assignments	Geometry
HL^1	380	26313	$n \longrightarrow \pi^*$	-
	250	40000	$\pi \longrightarrow \pi^*$	
HL^2	370	27027	$n \longrightarrow \pi^*$	-
	260	39462	$\pi \longrightarrow \pi^*$	
$[Mn(HL^1)_2Cl_2]$	560	17857	$^6A^1g \longrightarrow {}^4T^1g(4G)$	Octahedral
	410	24390	$^6A_1g \longrightarrow {}^4E_{2g}$	Octahedral
	340	29412	LMCT	Octahedral
$[Mn(HL^2)_2Cl_2]$	420	23809	$^6A_1g \longrightarrow {}^4E_{2g}$	Octahedral
	310	32258	LMCT	Octahedral
$[Fe(HL^1)_2Cl_2]Cl$	600	16667	$^6A_1g \longrightarrow {}^4E_{2g}$	Octahedral
	480	20833	$^6A_1g \longrightarrow {}^4E_{2g}$	Octahedral
	380	26316	LMCT	Octahedral
$[Fe(HL^2)_2Cl_2]Cl$	490	20408	$^6A_1g \longrightarrow {}^4E_{2g}$	Octahedral
	370	27027	LMCT	Octahedral

Table 4: The Antimicrobial Activity data for the Ligand and its Metal Complexes

Compound	Conc (µg/ ml)	S. pyogenes	B.subtilis	C. species	S.dysentriae	C.albicans
HL^1	30	$23.70\pm0.58^{a,a'}$	$13.00\pm0.00^{a,a'}$	24.70 ± 0.58^{a}	20.00 ± 1.00^{a}	$18.70\pm10.58^{a,a'}$
	20	18.70 ± 0.58^{b}	$9.700\pm0.58^{b,b'}$	$21.00\pm0.00^{b,b'}$	$14.70\pm0.58^{b,b'}$	$14.30\pm0.58^{b,b'}$
	10	14.30 ± 0.58^{c}	$7.00\pm0.00^{c,c'}$	$16.00\pm0.00^{c,b',c'}$	$11.00\pm0.00^{c,c'}$	$10.30\pm0.58^{c,c'}$
$[Mn(HL^1)_2Cl_2]$	30	$33.30\pm0.58^{d,d'}$	$13.00\pm0.00^{a,a'}$	$21.30\pm0.58^{d,b',c'}$	$20.70\pm0.58^{a,a'}$	$20.30\pm0.58^{d,d'}$
	20	$27.70\pm0.58^{e,e'}$	11.00 ± 0.00^{d}	$17.30\pm0.58^{e,b'}$	$16.30\pm0.58^{d,d'}$	$15.70\pm0.58^{e,b'}$
	10	$24.30\pm0.58^{a,a'}$	$7.70\pm0.58^{e,c'}$	12.70 ± 0.58^{f}	$12.30\pm0.58^{e,c'}$	$12.00\pm0.00^{f,b'}$
$[Fe(HL^1)_2Cl_2]Cl$	30	$32.30\pm0.58^{f,a'}$	$18.30\pm0.58^{f,f}$	$30.00\pm0.00^{g,,g'}$	$18.00\pm0.00^{f,f}$	$17.00\pm0.00^{g,,g'}$
	20	$27.00\pm0.00^{g,,e'}$	$14.00\pm0.00^{g,,a'}$	$24.70\pm0.58^{a,a'}$	$13.70\pm0.58^{g,,c',d'}$	$12.70\pm0.58^{h,b'}$
	10	21.70 ± 0.58^{h}	$9.30\pm0.58^{h,h'}$	$20.30\pm0.58^{h,b',c'}$	9.30 ± 0.58^{h}	$9.30\pm0.58^{i,c'}$
Trimethoprim	30	$35.00\pm0.00^{o,i'}$	$19.30\pm0.58^{i,b',f}$	$23.30\pm0.58^{a,a'}$	$23.00\pm0.00^{n,c',a'}$	$24.70\pm0.58^{p,j',n'}$
	20	$30.30\pm0.58^{p,j'}$	$14.30\pm0.58^{j,a'}$	$18.70\pm0.58^{m,b'}$	$18.30\pm0.58^{f,a',f}$	$20.70\pm0.58^{q,a',d'}$
	10	$27.00\pm0.00^{q,l'}$	$9.30\pm0.58^{k,h'}$	$15.00\pm0.00^{n,b'}$	$13.70\pm0.58^{b',b',c',d'}$	$18.00\pm0.00^{a,g'}$

*Different subscript letters along the same column are significantly ($P<0.05$) different.

Table 5: Minimum Inhibitory Concentration of the Ligand (HL') and its Complexes

Compound	Conc (µg/ ml)	Organisms				
		S. pyogenes	B. Subtilis	C. Specie	S. dysentriae	C. Albicans
HL^1	10	-	-	-	-	-
	8	-	-	-	-	
	6	-	+	-	-	+
	4	+	+	+	+	+
	2	+	+	+	+	+
$[Mn(HL^1)Cl_2]$	10	-	-	-	-	-
	8	-	-	-	-	
	6	-	+	-	-	-
	4	-	+	+	+	+
	2	+	+	+	+	+
$[Fe(HL^1)_2Cl_2]Cl$	10	-	-	-	-	-
	8	-	-	-	-	-
	6	-	-	-	+	+
	4	-	+	-	+	+
	2	+	+	+	+	+
Trimethoprim	10	-		-	-	-
	8	-		-	-	-
	6	-		-	-	-
	4	-		+	+	+
	2	+		+	+	+

Table 6: Minimum Bactericidal Concentration of the Ligand (MLI) and its Complexes

Compound	Conc (µg/ml	Organisms				
		S. pyogenes	B. Subtilis	C. Specie	S. dysentriae	C. Albicans
HL^1	10	-	-	-	-	-
	8	-	+	-	-	+
	6	+	+	+	+	+
	4	+	+	+	+	+
	2	+	+	+	+	+
$[Mn(HL^1)Cl_2]$	10	-	-	-	-	-
	8	-	+	-	-	-
	6	-	+	-	+	+
	4	-	+	+	+	+
	2	+	+	+	+	+
$[Fe(HL^1)_2Cl_2]Cl$	10	-	-	-	-	-
	8	-	-	-	-	-
	6	-	+	-	+	+
	4	-	+	-	+	+
	2	+	+	+	+	+
Trimethoprim	10	-	-	-	-	-
	8	-	+	-	-	-
	6	-	+	-	+	-
	4	-	+	+	+	+
	2	+	+	+	+	+

Table 7: The Antimicrobial Activity data for the Ligand (HL2) and its Metal Complexes

Compound	Conc (µg/ml)	S. pyogenes	B.subtilis	C. species	S.dysentriae	C.albicans
HL^2	30	30.30 ± 0.58^{a}	15.30 ± 0.58^{b}	27.30 ± 0.58^{b}	13.30 ± 0.58^{a}	$18.70\pm1.15^{a,a'}$
	20	$26.00\pm0.00^{a,a'}$	12.00 ± 0.00^{c}	$22.70\pm0.58^{a,a'}$	$10.30\pm0.58^{b,b'}$	$13.30\pm0.58^{b,b'}$
	10	$31.30\pm0.58^{b,a',b'}$	$9.00\pm0.00^{a,d}$	$18.30\pm0.58^{c,c'}$	$8.00\pm0.58^{c,c'}$	$9.70\pm0.58^{c,}$
$[Mn(HL^2)_2Cl_2]$	30	$33.30\pm0.58^{a,a'}$	17.30 ± 0.58^{e}	$19.00\pm0.00^{d,c'}$	$18.30\pm0.58^{d,d'}$	$21.70\pm0.58^{d,d'}$
	20	$25.00\pm0.58^{c,a],b'c'}$	13.30 ± 0.58^{f}	$14.70\pm0.58^{e,e'}$	13.30 ± 0.58^{a}	$17.00\pm0.00^{e,e'}$
	10	$20.30\pm0.58^{d,b'}$	$9.70\pm0.58^{a,a'}$	11.70 ± 0.58^{f}	$9.00\pm0.00^{e,b'c'}$	$12.70\pm0.58^{f,a'}$
$[Fe(HL^2)_2Cl_2]Cl$	30	$38.70\pm0.58^{a,a'e'}$	0.00 ± 0.00	$27.30\pm0.58^{a,a'}$	30.70 ± 0.58^{f}	$24.30\pm0.58^{g,,g'}$
	20	$34.30\pm0.00^{a,a'b'}$	0.00 ± 0.00	$21.70\pm0.58^{g,a'}$	$26.70\pm0.58^{g,}$	$20.00\pm0.00^{a,d'}$
	10	$30.00\pm0.00^{a,a',b'}$	0.00 ± 0.00	$15.70\pm0.58^{h,e'}$	$21.30\pm0.58^{h,h'}$	$15.30\pm0.58^{h,e'}$
Trimethoprim	30	$35.00\pm0.00^{a,a',e'd'}$	19.30 ± 0.58^{g}	$23.30\pm0.58^{n,a'}$	$23.00\pm0.00^{n,i'}$	$24.70\pm0.58^{m,g'}$
	20	$30.30\pm0.58^{a,a',e',b'bd'}$	14.30 ± 0.58^{h}	$18.70\pm0.58^{o,b'}$	$18.30\pm0.58^{o,d'}$	$21.30\pm0.58^{n,d'}$
	10	$27.00\pm0.0058^{a,a',c',b'b,d'}$	$9.30\pm0.58^{a,a'}$	$15.00\pm0.00^{p,e'}$	13.70 ± 0.58^{a}	$18.00\pm0.00^{a,e'd'}$

Table 8: Minimum Inhibitory Concentration of the Ligand 2 and its Complexes

Compound	Conc (µg/ ml	Organisms				
		S. pyogenes	B. Subtilis	C. Specie	S. dysentriae	C. Albicans
HL^2	10	-	-	-	-	-
	8	-	-	-	-	-
	6	-	+	-	+	+
	4	-	+	+	+	+
	2	+	+	+	+	+
$[Mn(HL^2)_2Cl_2]$	10	-	-	-	-	-
	8	-	-	-	-	-
	6	-	-	-	+	-
	4	-	+	+	+	+
	2	+	+	+	+	+
$[Fe(HL^2)_2Cl_2]Cl$	10	-		-	-	-
	8	-		-	-	-
	6	-		-	-	-
	4	-		+	-	+
	2	+		+	+	+
Trimethoprim	10	-		-	-	-
	8	-		-	-	-
	6	-		-	-	-
	4	-		+	+	+
	2	+		+	+	+

Table 9 : Minimum Bactricidal Concentration of the Ligand (HL^2) and its Complexes

Compound	Conc (µg/ ml	Organisms				
		S. pyogenes	B. Subtilis	C. Specie	S. dysentriae	C. Albicans
HL^2	10	-	-	-	-	-
	8	-	+	-	+	+
	6	-	+	-	+	+
	4	-	+	+	+	+
	2	+	+	+	+	+
$[Mn(HL^2)_2Cl_2]$	10	-	-	-	-	-
	8	-	+	-	-	-
	6	-	+	-	+	+
	4	-	+	+	+	+
	2	+	+	+	+	+
$[Fe(HL^2)_2Cl_2]Cl$	10	-	+	-	-	-
	8	-	+	-	-	-
	6	-	+	-	-	-
	4	-	+	+	-	+

	2	+	+	+	+	+
Trimethoprim	10	-	-	-	-	-
	8	-	+	-	-	-
	6	-	+	-	+	-
	4	-	+	+	+	+
	2	+	+	+	+	+

Results

The condensation reaction between salicyldehyde or benzaldehyde with trimethoprim in a molar ratio of 1:1 produced the Schiff base ligands (HL1 and HL2) respectively. The interaction between the Schiff base ligands and each of the metal(II) ions separately in 1:2 molar ratio(M:L) produced the metal(II) complexes of the respective metal(II) ions with a percentage yield ranging between 79-83% (Table1).

Infra-red spectra

The FTIR spectra provides valuable information regarding the nature of the functional group attached to the metal atom. The IR spectra of the free ligands and their complexes were determined in the 400- 4000cm^{-1} range (Raman *et al.,* 2001). In general, the ligands exhibited similar IR features due to trimethoprim (Table 2).

Electronic spectra

The electronic absorption spectroscopy is useful in ascertaining the nature of binding mode between metal and ligands through the vacant orbital of the metal. This interaction between metals and ligands is usually through the empty d or f orbital in transition metals, which can result to d-d or f-f transition in the visible region and also corresponds to a particular energy level of transition. However, the situation differs for metals without d-orbital or electrons in d-orbital. The electronic absorption spectral data of the ligands and their complexes are presented in Table 3.

Antimicrobial studies

The antimicrobial sensitivity study of the Schiff bases and their metal complexes was conducted using *in vitro* disc diffusion method against different strains of human pathogens (Table 4- 9).

Discussion

The ligands and their complexes were found to be stable at room temperature .They are insoluble in water but soluble in methanol and ethanol. The molar conductance measurement of the complexes in methanol (10^{-3} M) at 25 ˚C revealed their non-electrolytic nature (0.11 – 0.28 $Scm2mol^{-1}$). The insolubility of these complexes in water and their nonelectrolytic nature suggests that they are probably nonpolar. The colours of the complexes are typical of transition metal complexes which are attributed to d-d transitions of electrons between energy levels because of partially filled d orbital or charge transfer transitions. The melting points of

the Schiff bases and the metal (II) complexes are sharp and are in the range of 232- 242ºC and 255-285ºC respectively. The high melting points indicates that the compounds are stable and not easily decomposed. The higher melting points of the complexes also suggest the 'chelating effect' of the respective ligands. Chelating ligands form more stable complexes than do an equivalent number of related monodentate ligands.

A broad band at the region of 3406 and 3462 cm^{-1} in HL^2 and HL^1 respectively is assigned to NH_2 vibration in the free ligand. These bands shifted to the lower frequency at about 3398 – 3402 cm^{-1} in all the complexes, this slight shift indicates that the metal ion have coordinated to the trimethoprim Schiff bases through the nitrogen atom of –NH and –NH groups. This was further confirmed with the appearance of (M-N) band at the region of 489 -524 cm^{-1} in the spectra of the complexes . The spectral data of the ligands also confirmed the formation of imines bond υ (-C=N-H) and the absence of carbonyl bond υ (C=O). A sharp frequency band at 1637 and 1643 cm^{-1} in trimethoprim Schiff bases (HL^1 and HL^2) were assigned to the pyrimidine nitrogen (azomethine) , υ (C=N) [24]. This band was shifted to higher frequencies in all the complexes except of $MnHL^1$, this slight increase in the (C=N) absorption band suggest the. The presence of new bands in the spectra of the metal complexes in the far infrared region at 489-524 cm^{-1} due to the υ (M-N) vibrations supports the coordination of the imine nitrogen to the metal ion.

From the results obtained, the ligands absorbed in the region of 250 – 380 nm which corresponds to 40000 – 26316 cm^{-1} energy level assignable to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ respectively. The broad bands observed in the visible region are due to d-d transitions of the metal ion.

From the results obtained on antimicrobial studies, the ligand (HL^1) and its complexes did not show much effect against the bacterial isolates as well as the fungus *Candida albicans* tested as compared with the standard trimethoprim drug at all concentrations with the exception of $Fe(HL^1)_2 Cl_2$]Cl which indicated susceptibility with zone of inhibition of 30.00 mm (30 µg/ml), 24.70 mm (20 µg/ml) and 20.30 mm (10 µg/ml) against *Corynaebacterium specie* compared to 23.30 mm (30 µg/ml), 18.7 mm (20 µg/ml) and 15.00 mm (10 µg/ml) shown by the parent drug trimethoprim . In contrast, HL2 complexes showed greater activity against *Streptococcus pyogenes*, *Corynaebacterium specie* and *Shigella dysentriae* at all concentrations compared to the trimethoprim standard. $Mn(HL^2)Cl_2$ complex showed low to moderate activity against all the tested organisms. $Fe(HL^2)_2 Cl_2$]Cl did not show any visible inhibition against *Bacillus subtilis* Table 7. Antimicrobial resistance against some promising antibiotics drugs such as trimethoprim and others was commonly observed in many countries worldwide during *in vivo* analysis of pathogens. The minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) of the compounds were evaluated and compared with the standard trimethoprim as presented in the Tables 5-9. The complexes of HL^1 and HL^2 showed MIC and MBC values between 4µl/ml. The overall results indicated that Fe(III) complexes are more active than the Mn(II) complexes. The lowest values of 4 µl/ml was recorded for $Fe(HL^1)_2Cl_2$]Cl against *Corynaebacterium species* and $Fe(HL^2)_2Cl_2$]Cl against *Shigella dysentriae*, The standard drug (trimethoprim) revealed MIC and MBC of 6 µl/ml on same organism.

The results of this work showed that the synthesized compounds are pure because of their sharp melting points, while the low conductivity values suggested that the complexes are non-electrolytes. The percentages of metals obtained were in close agreement to the theoretical values. The spectroscopic data obtained confirm the coordination between the ligands and metals. Antimicrobial susceptibility test, MIC and MBC results showed that Fe(III) complexes are more active than the Mn(II) complexes when compared with the standard trimethoprim drug.

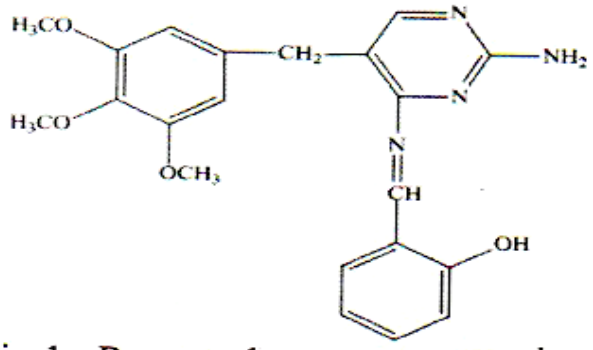

Fig 1 : Proposed structure of HL^1

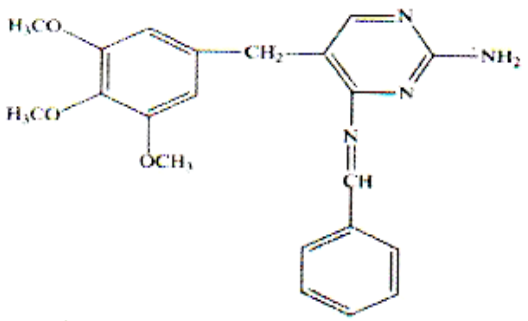

Fig 2: Proposed structure of HL^2

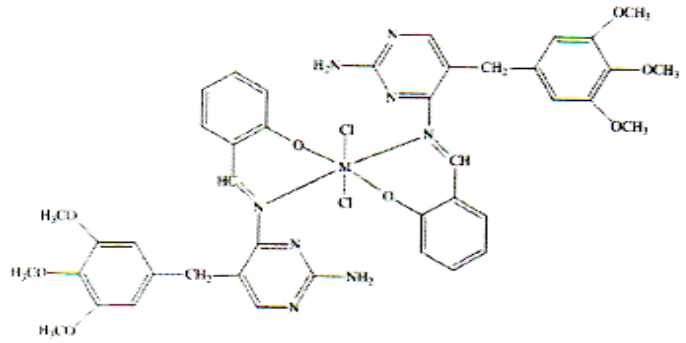

Fig 3: Proposed structure of $[Mn(HL^1)_2Cl_2]$

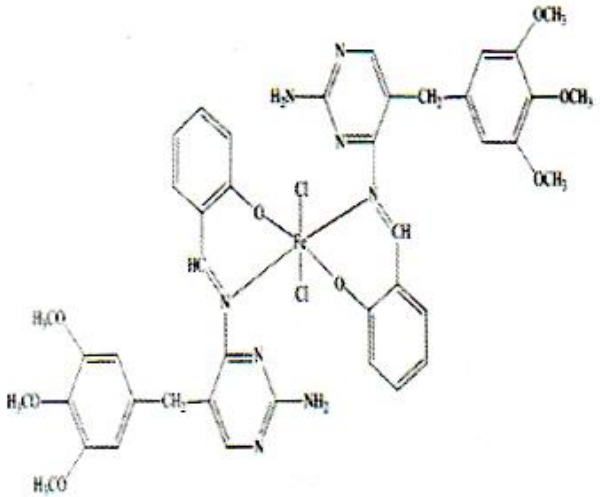

Fig 4: Proposed structure of $[Fe(HL^1)_2Cl_2]Cl$

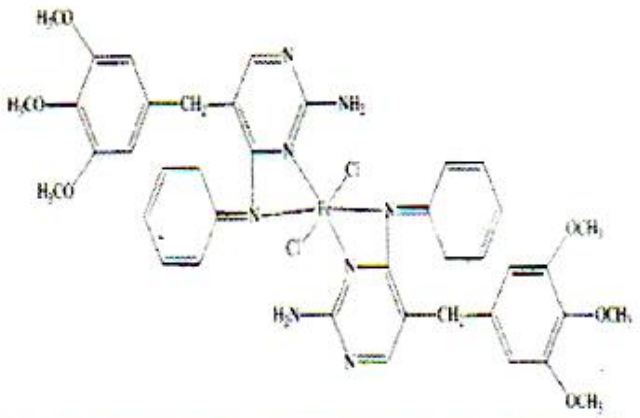

Fig5:Proposed structure of $[Mn(HL^2)_2Cl_2]Cl$

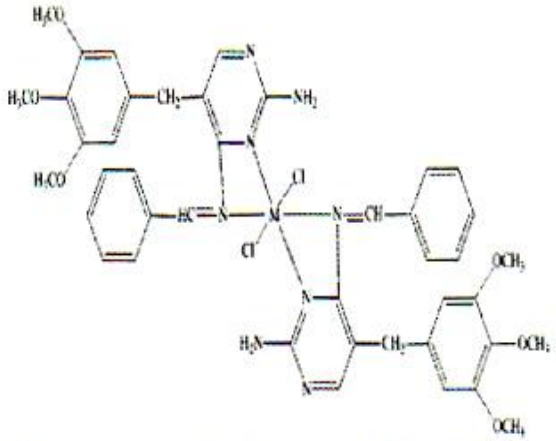

Fig6:Proposed structure of $[Fe(HL^2)_2Cl_2]Cl$

Acknowledgements

I am very much grateful to Prof. Rabindra Singh, HOD, Dept. of Chemistry, J.P. University, Chapra, Prof. Udai Arvind, Dean Science, J.P. University, Chapra, Prof. U.S. Yadav, former HOD, Deptt. Of Chemistry, J.P. University, Chapra, Dr. Sanjay Kr., Associate Prof. Deptt. Of Chemistry, Jagdam College, Chapra for their innovative and valuable suggestions and moral support for the same.

References

1. Neelima M, Kavita P, Sarvesh KS, Dinesh K (2016). Synthesis, Characterization and Antimicrobial activity of Schiff base Ce (III) Complexes. *Polyhedron*. 120, 60–68.
2. Mohammad S, Summaiya H, Mohammed S, Owais M, Mohammad A, Saud, IA (2016). Pharmacophore hybrid Approach of New Modulated bis-diimine CuII/ZnII Complexes based on 5-chloro Isatin Schiff base Derivatives: Synthesis, Spectral Studies and Comparative Biological Assessment. *Journal of Photochemistry & Photobiology*. 157, 39–56.
3. Yousef E, Barbara M, Maryam M, Moj K (2017). A Novel Cationic Cobalt (III) Schiff base Complex: Preparation, Crystal Structure, Hirshfeld Surface Analysis, Antimicrobial Activities and Molecular docking. *Journal of Microbial Pathogenesis.* 113, 160–167.
4. Hina Z, Anis A, Asad UK, and Tahir AK (2015). Synthesis, Characterization and Antimicrobial Studies of Schiff base Complexes. *Journal of Molecular Structure.* 1097**,** 129–135.
5. World Health Organization (2014). Antimicrobial Resistance, Global Report on Surveillance, WHO Library Cataloguing-in-Publication Data
6. Golkar Z, Bagazra O, Pace DG (2014). Bacteriophage Therapy: A Potential Solution for the Antibiotic Resistance Crisis. *Journal of Infectious Diseases*. 8(2), 129–136.
7. Spellberg B, Gilbert DN (2014). The future of Antibiotics and Resistance: A Tribute to a Career of Leadership by John Bartlett. *Journal of Clinical Infectious Diseases.* 59, 71–75.
8. Gould IM, Bal AM (2013). New Antibiotic Agents in the Pipeline and how they can Overcome Microbial resistance. *Virulence*. 4(2), 185–191.
9. Wright GD (2014). Something new: Revisiting Natural Products in Antibiotic Drug Discovery, *Canadian Journal of Microbiology*. 60(3), 147–154.
10. Cook BM, Mohandas N, Copel RL (2004). Malaria and the Red Blood Cell Membrane. *Seminars in Hematology*. 41, 173–188.
11. Ajibade PA , and ZuluNH (201 0) . " Synthesis , Characterization, and Antibacterial Activity of Metal Complexes of Phenylthiourea: The X-ray Single Crystal Structure of [Zn(SC(NH)NHC H) (OOCCH)] C H OH," 2 6 5 2 3 2 2 5 *Journal of Coordination Chem*istry. 63(18), 3229–3239.
12. I Waziri, MB, Fugu and NP Ndahi (2018). Solvent-free Synthesis, Characterization and Antimicrobial Studies of Calcium and Potassium Complexes with Some Cephalosporin Antibiotics. *Research Journal of Chemical Science.* 8(6), 8 -15.
13. Hussein BHM, Hassan AA, Mona FEA, Abdullah IEF (2012). A novel Anti-tumor Agent, Ln (III) 2-thioacetate Benzothiazole Induces Anti-angiogenic Effect and Cell death in cancer cell lines. *European Journal of Medicinal Chemistry*. 51, 99–109.
14. Aurora R, Mariana CC, Emilia A, and Cezar IS (2014). Transition Metal(II) Complexes with Cefotaxime-Derived Schiff Base: Synthesis, Characterization, and Antimicrobial Studies, *Journal of Bioinorganic Chemistry And Applications.* 1-17.

15. Mounika K, Anupama B, Pragathi J and Gyanakumari C (2010). Synthesis, Characterization and Biological Activity of a Schiff Base Derived from 3-Ethoxy Salicylaldehyde and 2-Amino Benzoic acids and its Transition Metal Complexes. *Journal of Science Research.* 3, 513-524.
16. Ndahi NP and Wakil MI (2015). Synthesis, Characterization and Antimicrobial Studies of Metal (II) Complexes Derived from 2,4-Dihydroxybenzophenone with Ethylenediamine, *Bulleting of pure and applied Science*. 34c(1-2), 1-9.
17. Osowole AA (2008). Synthesis and Characterization of Some Tetradentate Schiff Base Complexes and Their Hetroleptic Analogues. *European Journal of Chem*istry. 5(1), 130 – 135.
18. Shayma AS, Yang F and Abbas SA (2009). Synthesis and Characterization of mixed Ligand Complexes of 8- hydroxyquinoline and O-hydroxybenzylidene-1-phenyl-2- 3-dimethyl-4-amino-3 pyrazolin-5-one with Fe(II), Co(II), Ni(II), and Cu(II) ions. *European Journal Science Research.* 33, 702-709
19. Osowole AA and Wakil SM (2015). Synthesis, Characterization and Antimicribial Activity of Some Mixed Trimethoprim-Sulfamethoxazole Metal Complexes. *World Applied Science Journal.* 33(2), 336-342.
20. Sunil J, Vatsala P and Uma V(2010). Antibacterial Properties of Mn(II), Co(II), Ni(II) and Zn(II) Complexes Drived from Schifff Base Trimethoprim. *Der pharma chemical.* 2(5), 329-336.
21. Raman N, Raja YP and Kulandaisamy A(2001). Synthesis and Characterisation of Cu(II), Ni(II), Mn(II), Zn(II) and VO(II) Schiff Base Complexes Derived From o- Phenylenediamine and Acetoacetanilide. *Journal of Chemical Science.* 113(3), 183-189.
22. Demirezen N, Tarınç D, Polat D, Çeşme M, Gölcü A, and Tümer M (2012). Synthesis of Trimethoprim Metal Complexes: Spectral, Electrochemical, Thermal, DNABinding and Surface Morphology Studies. *Spectrochimica Acta Part A: Molecilar and Biomolecular Spectroscopy.* 94, 243–255.
23. Xavier A and Srividhya N(2014): Synthesis and Study of Schiff Base Ligands, *Journal of Applied Chemistry. (IOSRJAC).* 7(11), 6-15.
24. Contini G, Ciccioli A, Cozza C, Barbaro M, and Marabini M(1997). Infrared Study of 2-Mercaptobenzothiazole and Two of its Derivatives Adsorbed on PbS. *International Journal Mineral Process.* 51(1-4), 283-289.
25. Peter A A and Omoruyi GI (2013). Synthesis, Characterization, and Antibacterial Studies of Pd(II) and Pt(II) Complexes of Some Diaminopyrimidine Derivatives, , *Bioinorganic Chemistry and Applications.* 1, 1-8.
26. Gulcan M, Sonmez M and Berber I (2012). Synthesis, Characterization and Antimicrobial Activity of a New Pyrimidine Schiff Base and its Cu(II), Ni(II), Co(II), Pt(II) and Pd(II) Complexes. *Turkish Journal of Chem*istry. 36**,** 189-200.
27. Raheem TM, Al-Noor TH and Ismail AH (2014). Preparation, Characterization, and Antibacterial Properties of Mixed Ligand Complexes of L-leucine and Sulfamethoxazole (Antibiotic) with Mn(II),

Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) ions. *Journal of Advcances in Physics Theories and Applications*. 27, 8-19.

28. Mahasin Al, Huda K and Carolin S (2014). Synthesis, Physical Characterization and Biological Evaluation of Schiff base M(II) Complexes, *Journal of the Association of Arab Universities for Basic and Applied Sciences*. 15, 28–34

29. Rahman M, Shoma S, Rashid H, Arifeen SE, Baqui AH, Siddiquel, AK, Nair GB, Sack DA, (2007). Increasing Spectrum in Antimicrobial Resistance of Shigella isolates in Bangladesh: Resistance to azithromycin and ceftriaxone and decreased susceptibility to ciprofloxacin. *Journal Health Population and Nutr*ition. 2, 158–167.