

SYNTHESIS, SPECTROSCOPIC AND BIOLOGICAL CHARACTERIZATION OF SOME TRANSITION METAL COMPLEXES WITH ETHYL 2-[(2E, 3Z)-4-HYDROXPENT-3-EN-2-YLIDENE] AMINO}-4, 5, 6, 7-TETRAHYDRO-1-BENZOTHIOPHENE-3-CARBOXYLATE

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ABSTRACT

Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes with a tridentate Schiff base prepared by condensation of ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate with (3Z)-4-hydroxypent-3-en-2-one were synthesized and characterized on the basis of elemental analysis, molar conductance measurements, magnetic susceptibility values, UV-Vis, IR, EPR and NMR spectral data wherever possible. Spectral studies show that the ligand behaves as tridentate chelating agent and bonded to the metal ion through azomethine nitrogen, ester carbonyl and enolic oxygen atom. Electronic spectra and magnetic susceptibility measurement reveal octahedral geometry for Ni (II) and Co (II) complexes, tetrahedral configuration for Mn (II) and Zn (II) complexes, and square planar dimer structure for Cu (II) complex. The complexes are found to be non-electrolytic in nature on the basis of low molar conductance. These metal complexes were also screened for its antibacterial activity against pathogenic strains causing urinary tract infections and were found to be effective.

KEY WORDS

Tridentate, Schiff base, Antibacterial.

INTRODUCTION

Metal-organic chemistry is becoming an emerging area of research due to the demand of new metal based antibacterial and anti fungal compounds [1, 2]. The aliphatic or aromatic compounds can form strong five or six membered chelates rings which are able to produce the metal containing cross-linking agents with required properties [3]. Benzothiophene systems and their substituted derivatives have attracted a great deal of interest over the years [4]. Their aromatic character contributes to their reactivity, stability and chemical and electronic properties. A vast number of heterocyclic derivatives observed in natural products have been reported [5]. On the other side, they find increasing application as superconductors [6, 7], optoelectronics [8, 9], light emission diodes LEDs, and non-linear optical (NLO) chromophores [10, 11]. In addition, they also exhibit several biological properties including antibacterial

activity against various pathogenic and non pathogenic bacteria [12-14]. In this era where we face threats in the form of Multi drug resistant pathogens evolving into super bugs like Extended Spectrum β -lactamase (ESBL) and Metallo- β -lactamase (MBL) producers capable of hydrolyzing β -lactam antibiotics, screening of antimicrobial properties of these complexes will provide a novel approach in the field of pharmacy [15].

In this investigation substituted 2-amino thiophene namely ethyl 2-amino-4, 5, 6, 7 tetrahydro benzo (b) thiophene 3-carboxylate has been condensed with (3Z)-4-hydroxypent-3-en-2-one to form a potentially tridentate ligand viz ethyl 2-[(2E,3Z)-4-hydroxypent-3-en-2-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate have been synthesized and characterized by their elemental analysis, UV, IR and NMR studies. This ligand were used to synthesize Mn(II), Co(II), Ni(II) Cu(II) and Zn(II) complexes. The

complexes were characterized by elemental analysis, magnetic moments, Molar conductance, along with electronic, infrared and NMR spectral analysis. The antibacterial activities of these metal complexes have been screened against ESBL (Extended spectrum β -lactamase) and MBL (Metallo- β -lactamase) producers which are able to hydrolyze β -lactam antibiotics including 3rd generation cephalosporins and carbapenems.

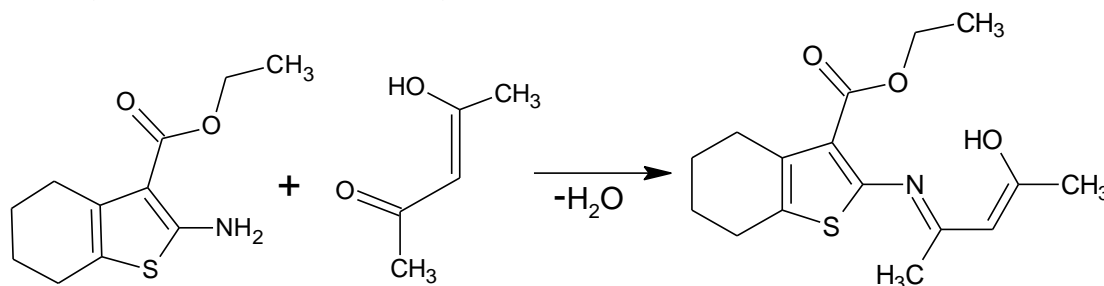
MATERIALS AND METHODS

All chemical used in the project work were of AR grade and recrystallised while the solvent were purified and double distilled before use. Metal content was determined by the standard methods [16]. Molar conductance was measured in DMF (10^{-3} M solution) on an ELICO Digital Conductivity meter Model CM-180. The electronic spectra of the complex in DMF were recorded on UV-Systronic spectrophotometer. The IR spectra were recorded in KBr disc on a Perkin Elmer Model 1600 FTIR Spectrophotometer, where as the presence of $\nu(\text{M-Cl})$ in complexes was recorded on Plytec 30

spectrometer using CsI disc. The $^1\text{H-NMR}$ Spectra was recorded in DMSO on a VXR-300S Varian Supercon NMR Spectrometer using TMS as the internal reference. Magnetic Susceptibility measurements were carried out by employing the Gouy method using $\text{Hg} [\text{Co} (\text{SCN})_4]$ as a calibrant. . The EPR spectrum of the copper (II) complex was recorded using a Varian-112EPR spectrometer using DPPH as reference material.

Preparation of ligand:

Ethyl 2-[[[(2*E*,3*Z*)-4-hydroxypent-3-en-2-ylidene]amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate: Ethyl 2-amino-4, 5, 6, 7 tetrahydro benzo(b)thiophene 3-carboxylate is prepared according to a reported method [17]. To a solution of this thiophene derivatives (0.01mol) in ethanol (20ml) was added to a solution of (3*Z*)-4-hydroxypent-3-en-2-one (0.01mol) in ethanol (10ml) in small portion with constant stirring. The resulting solution was refluxed on a water bath for about four hours. On cooling the solution, the Schiff base crystallized. It was then filtered, washed and sucked dry. Further purification was done by crystallization from ethanol (MP 142°C).



Scheme

Preparation of metal complexes: The metal complexes were prepared by the following general procedure. To a magnetically stirred and warmed ethanolic solution (20ml) of the ligand (0.01mol) added an ethanolic solution of metal (II) chloride in appropriate ratios dissolved in ethanol (10ml) in small parts. After complete additions of the metal salt solution, the pH was adjusted to 7.5 by adding ethanolic ammonia. It was then refluxed for about six

hours in a water bath and the resulting solution was reduced to half the initial volume and allowed to stand overnight. The complex formed was filtered, washed successively with aqueous ethanol and ether. Finally the complex was dried in vacuum over P_4O_{10} .

Test organisms used in the study: 19 MDR (Multi-Drug Resistant) gram negative uropathogens were used in the study including 6 ESBL (Extended spectrum β -lactamase) and 7 MBL (Metallo- β -lactamase) producers (**Table-1**).

Table-1: Test organisms used in the study

ESBL Producing uropathogens	MBL Producing uropathogens	Non-ESBL and MBL Producing MDR uropathogens
<i>E.coli</i> strain 1	<i>E.coli</i> strain 1	<i>Proteus vulgaris</i>
<i>Citrobacter diversus</i> strain 1	<i>E.coli</i> strain 2	<i>Proteus mirabilis</i>
<i>E.coli</i> strain 2	<i>Pseudomonas aeruginosa</i>	<i>E.coli</i>
<i>Pseudomonas aeruginosa</i>	<i>E.coli</i> strain 3	<i>Morganella morganii</i>
<i>Citrobacter diversus</i> strain 2	<i>Klebsiella pneumonia</i> strain 1	<i>C.diversus</i>
<i>Proteus vulgaris</i>	<i>Klebsiella pneumonia</i> strain 2	<i>Pseudomonas aeruginosa</i>
	<i>C.diversus</i>	

Antimicrobial susceptibility of uropathogens:

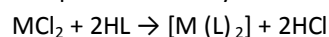
Antibiotic sensitivity test of the pathogens was carried out using Kirby Bauer method so as to obtain Antibiogram pattern [18].

Antibacterial activity:

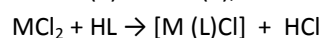
Antibacterial activity of the metal complexes was determined by Agar cup method. The metal complexes were dissolved in HPLC grade ethanol to obtain final concentration of 200 µg/µl. A loopful of the test isolates were inoculated in 10 ml of Brain Heart infusion (BHI) broth and incubated at 37°C for 24 hours in order to obtain actively growing log phase isolates. Sterile 20 ml of Luria Bertani agar was melted cooled to around 40°C and 0.4 ml test strain (0.1 O.D. at 530nm) was seeded and poured into a 9cm diameter aneubra Petri plates. Using a sterile cork borer (8 mm in diameter), wells was punched in each plate after solidification of the medium. 50 µl of the test sample (metal complex) was then added to the wells and incubated at 37°C for 24 hours to observe the zones of inhibition against each metal complex. Control wells were also set up using 50 µl of ethanol (solvent) for each isolate. The mean value obtained for three individual replicates was used to calculate the zone of inhibition for each isolate [19].

RESULTS AND DISCUSSION

Analytical data indicated that ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate condensed with (3Z)-4-hydroxypent-3-en-2-one in 1:1 molar ratio and the product formed well defined complexes with the metal salts. Formation of the complexes can be symbolized as follows:



M= Co (II) and Ni (II),



M= Mn(II), Zn(II)



M= Cu (II)

HL=ethyl 2-[[[(2E, 3Z)-4-hydroxypent-3-en-2-ylidene] amino]-4, 5, 6, 7-tetrahydro-1-benzothiophene -3-carboxylate

Formulation of the complexes has been based on their elemental analytical data, molar conductance values and magnetic susceptibility data. The stiochiometry of the complexes 1:1 (Metal: ligand) of Mn (II), Cu (II) and Zn (II) complexes, where as 1:2 (metal: ligand) of Co (II) and Ni (II) complexes. All complexes are brightly coloured, non hygroscopic and decomposed above 180°C. The molar conductance values support the non-electrolyte nature of the metal complexes [20] as shown in **Table-2**

Table-2: Physico-chemical characteristic of schiff base ligand and its metal complexes

Compound	Colour	F.Wt	Elemental analysis (%)					Molar Cond. ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$)
			Found(calcd)					
			C	N	S	Cl	M	
HL	yellow	307.41	62.51 (63.02)	4.56 (3.86)	10.43 (9.56)	-	-	-----
[Mn(L)Cl]	Satin brown	396.79	48.43 (47.98)	3.53 (3.64)	8.08 (7.46)	8.93 (9.29)	13.85 (12.48)	2.53
[Co(L) ₂]	Timber brown	671.73	57.22 (56.62)	4.17 (5.30)	9.55 (9.41)		8.77 (7.16)	5.68
[Ni(L) ₂]	brown	671.49	57.24 (56.04)	4.17 (5.14)	9.55 (8.88)		8.74 (8.53)	3.62
[Cu(L)Cl] ₂	black	810.79	47.40 (45.89)	3.46 (4.56)	7.91 (7.00)	8.75 (9.25)	15.67 (14.26)	5.67
[Zn(L)Cl]	midbuff	407.26	47.19 (46.35)	3.44 (2.96)	7.87 (6.55)	8.71 (9.04)	16.06 (15.21)	6.46

The UV spectral bands characteristic of the ligand is only marginally red shifted in the spectra of the metal complexes indicating that no structural alteration of the ligand occurs on coordination with the metal ions. In the metal complexes, the $\nu(\text{C}=\text{N})$ is displaced to lower wave number by about 20-30 cm^{-1} on bond stabilization of the azomethine moiety upon coordination. The bond corresponding to the ester $\nu(\text{C}=\text{O})$ has been shifted to lower frequency by about 30-35 cm^{-1} in the metal complexes indicating coordination by ester function [21]. A broad band at 3200 cm^{-1} which is assigned to the enolic OH group of the (3Z)-4-hydroxypent-3-en-2-one moiety. the broadness of this band indicates the presence of hydrogen bond. this band disappears in the complexes

indicates deprotonation of enolic group, which lead to a six-membered ring structure around metal ions. A strong band around 2930 cm^{-1} due to $\nu(\text{C}-\text{H})$ of cyclohexane did not show any appreciable change in metal complexes. Infra spectra of the complexes also showed non-ligand band in the region 430-460 cm^{-1} and 510-520 cm^{-1} , which could be assigned to $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ modes respectively [22]. The medium band observed in the range 385- 395 cm^{-1} can be assigned to the presence of $\nu(\text{M}-\text{Cl})$ in complexes [23] which was recorded on Plytec 30 spectrometer using CsI disc. Absence of $\nu(\text{M}-\text{S})$ band in the far infrared spectra of the metal complexes gives direct evidence to non-involvement of ring sulphur in bond formation (Table-3).

Table -3: Important IR spectral bands of Schiff base and its metal complexes

HL	[Mn(L)Cl]	[Co(L) ₂]	[Ni(L) ₂]	[Cu(L)Cl] ₂	[Zn(L)Cl]	Tentative assignment
3200br	----	---	---	----	----	$\nu(\text{O}-\text{H})$
2930m	2932m	2931w	2935m	2930m	2930w	$\nu(\text{C}-\text{H})$
1700s	1670s	1665s	1668s	1672s	1668s	$\nu(\text{C}=\text{O})$
1658s	1634s	1620s	1632s	1619s	1635s	$\nu(\text{C}=\text{N})$ azomethine
608s	608m	609s	608s	609m	608s	$\nu(\text{C}=\text{S})$
---	550m	570m	605m	610m	590m	$\nu(\text{M}-\text{O})$
---	510m	517m	518m	519m	510m	$\nu(\text{M} \leftarrow \text{O})$
---	430m	445m	460m	457m	448m	$\nu(\text{M} \leftarrow \text{N})$
---	382m	---	---	395m	385m	$\nu(\text{M}-\text{Cl})$

HL= ethyl 2-[(2E, 3Z)-4-hydroxypent-3-en-2-ylidene] amino-4, 5, 6, 7-tetrahydro-1-benzothiophene-3-carboxylate

Proton NMR spectral data of the ligand supported the conclusion drawn on the basis of UV and IR spectral data. The absence of NH_2 proton signal in the NMR spectrum of ligand in DMSO-d_6 indicates successful Schiff base formation by replacement of the C=O group of (3Z)-4-hydroxypent-3-en-2-one. A signal at 13.2 δ indicates the enolic proton and therefore the weakest shielded proton in the molecule. The disappearance of the signal at 13.2 δ was confirmed to the fact that the ligand underwent deprotonation of the enolic OH group during complexation with the metal ions. The signal at 1.50 δ (d) and 4.30 δ (m) can be assigned for methyl and methylene proton respectively of the ester group. Two multiplets centered at 2.6-2.7 δ and doublet at 1.2 δ in the ligand and metal complexes are due to different hydrogen atom of the tetrahydro benzo thiophene ring. A signal at 5.8 δ and 2.0 δ is due to methine and two methyl group proton respectively.

The electronic absorption spectrum of the ligand in alcohol showed three band at 285, 340 and 360 nm. The first one may be assigned to intraligand $\pi \rightarrow \pi^*$ transition which is nearly unchanged on complexation, whereas the second and third band may be assigned to the $n \rightarrow \pi^*$ and charge transfer transition of the azomethine and ester C=O group [24, 25]. It is found that these bands were shifted to lower energy on complexation, indicating participation of this group in coordination with the metal ions. In addition, the spectra of the complexes showed new bands observed in the 420-440 nm range which may be attributed to the charge transfer transitions.

The electronic spectra from $^6\text{A}_1$ ground state of Mn(II) complex to higher energy state are spin forbidden and thus transition are not observed in the spectrum of the Mn(II) complex. The electronic spectrum of Co(II) show absorption band at 9100, 14950 and 18500 cm^{-1} attributed to the transition $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{2g}(\text{F})(\text{u}_1)$, $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{A}_{2g}(\text{F})(\text{u}_2)$ and $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{1g}(\text{P})(\text{u}_3)$ respectively. This confirms octahedral geometry for the Co(II) complex [26]. The u_3/u_1 value in the Co(II) complex is 2.03 and it lies in the usual range (2.00-2.80) reported of octahedral complex. The electronic parameters were calculated using the standard

method [27, 28] and the values are as follows $\text{Dq}=1019\text{cm}^{-1}$, $\text{B}=699.4\text{cm}^{-1}$, $\beta = \text{B}'/\text{B}=0.72$, $\beta^0 = 28\%$ and $\text{CFSE} = -99.97 \text{ KJmol}^{-1}$. The low value of Racah parameters compare to the free ion value of 971 cm^{-1} β^0 value of 28% indicates the covalent nature of Co-L bond. The spectrum Ni(II) complex shows three absorption band 10150, 17600 and 28150 cm^{-1} , which may be assigned to the $^3\text{A}_{2g}(\text{F}) \rightarrow ^3\text{T}_{2g}(\text{F})(\text{u}_1)$, $^3\text{A}_{2g}(\text{F}) \rightarrow ^3\text{T}_{1g}(\text{F})(\text{u}_2)$ and $^3\text{A}_{2g}(\text{F}) \rightarrow ^3\text{T}_{1g}(\text{P})(\text{u}_3)$ transition respectively indicating octahedral geometry. The u_2/u_1 value in the Ni(II) complex is 1.73 and it lies in the range (1.60-1.82) for octahedral Ni(II) complexes. The electronic spectral parameters values are as follows $\text{Dq}=1015\text{cm}^{-1}$, $\text{B}=944 \text{ cm}^{-1}$, $\beta = \text{B}'/\text{B}=0.92$, $\beta^0 = 8\%$ and $\text{CFSE} = -145.51 \text{ KJmol}^{-1}$. The low value of Racah parameters compare to the free ion value of 1030 to 944 cm^{-1} of the complex and β^0 value of 8% indicates the covalent nature of Ni-L bond. The spectrum of Cu(II) complex shows a broad band at 18790 cm^{-1} attributed to $^2\text{B}_{1g} \rightarrow ^2\text{A}_{1g}$ transition which strongly favours the square planar geometry around the central metal ion [29]. The broadness of the band indicates distorted square planar geometry. The Zn(II) complex is diamagnetic and there is no d-d transition. The elemental analyses are in good agreement with the proposed formula suggesting tetra-coordinated Zn(II) complex preferred tetrahedral geometry [30].

Magnetic susceptibility measurements: magnetic moment of Mn(II) complex is 5.28 BM which shows the presence of five unpaired electrons. Magnetic moment of Co(II) and Ni(II) complex are 4.72 BM and 3.20 BM respectively indicates an octahedral configuration. The magnetic moment of the Cu(II) complex is 1.53 BM, which is below the expected value. This may be due to some antiferromagnetic interaction of two Cu(II) centres [31].

The room temperature ESR spectra recorded on polycrystalline Cu(II) complex. The ESR parameters are summarized in table 3. The observed g_{\parallel} value are less than 2.3 indicates the covalent character of the metal-ligand bond [32]. The trend $g_{\parallel} > g_{\perp} > g_e$ (2.0023) observed for this complex shows that the unpaired electron is localized in $\text{d}_{x^2-y^2}$ orbitals of the Cu(II) ion and the spectral features are characteristic

of axial symmetry tetragonally elongated structure of Cu(II) complex[32]. The axial factor G (given by $g_{\perp} - 2/g_{\parallel} - 2$) is greater than 4, indicating absence of exchange coupling [32]. The α^2 value suggests

appreciable covalent character in the bond. It is important to note that A_{\parallel} value nearly half of monmer value, such a situation is expected for Cu(II) dimer[33].

Table-4: ESR spectral parameters of Cu (II) complex

Complex	g_{\perp}	g_{\parallel}	g_{av}	α^2	λ	$A_{\parallel} \times 10^{-4}$	G
[Cu(L)Cl] ₂	2.02	2.08	2.04	0.38	177.4	87.8	4.32

Antimicrobial susceptibility testing using Kirby Bauer method of gram negative uropathogens was carried out and it was found that these uropathogens were resistant to most of the antibiotics as shown in Table-5. All isolates were found to be Multiple Drug Resistant (Resistant to more than 3 antibiotics) including 3rd generation Cephalosporins (Ceftazidime, Cefotaxime and Ceftriaxone). The effect of metal complexes on these test isolates are shown in table-6 below. Ethanol (solvent) did not show any zone of inhibition against the test organisms. However zirconium and vanadium showed considerable zones of inhibition in its complex form as compared to ligand. The antibacterial activity of these complexes can be attributed to its lipophilic nature which may

allow easy binding and penetration of the complex in the cellular structure of the pathogens. It can also be explained with the help of the concept of chelation, which reduces the polarity of the metal ion. As the positive charges of the metal are partially shared with the donor atoms present in the ligands and there is possible π -electron delocalization over the metal complex formed, the lipophilic character of the metal chelate increases and favors its permeation more efficiently through the lipid layer of the microorganism, thus destroying them more forcefully. The other factors like solubility and bond length between the metal and ligand may also increase the activity [15].

Table-5: Antibiotic resistance profile of the uropathogens

Isolates	Antibiotic resistance profile		
	ESBL Producing uropathogens		
	Sensitive	Intermediate	Resistant
<i>E.coli</i> strain 1	AS, AK, GF		BA, CF, PC, CH, RC, CI, TE, ZN, GM, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Citrobacter diversus</i> strain 1	AS, BA, CH		CF, PC, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>E.coli</i> strain 2	AS, CH, AK, GF	ZN	BA, CF, PC, RC, CI, TE, GM, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Pseudomonas aeruginosa</i>	CH, AK, GF		AS, BA, CF, PC, RC, CI, TE, ZN, GM, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Citrobacter diversus</i> strain 2	ZN, AK, GF	NX, CU, CP, PB, AS, CF, RC, GM	BA, PC, CH, CI, TE, TT, OX, RP, ZX, CB, NA, AG, FG BA, CF, CH, CI, TE, ZN, OX, ZX, CB, NA, AG, CU, CP, FG, PB
<i>Proteus vulgaris</i>	NX, AS, GM, AK	TT, RP, PC, RC, GF	

Non- ESBL and MBL Producing uropathogens			
<i>Proteus vulgaris</i>	AK, LOM, SPX, NET, CAZ, CIP, CPX, GEN, A/S, CZX, OF, PF, NX, CTR, CPZ, CTR, CFM, CPO, CPM		NA
<i>Proteus mirabilis</i>	CI, CF, BA, PB, CU, TT, AG, CP, TE, NA, NX, OX AK		GF, GM, ZN, RC, CH, PC, AS, FG, CB, ZX, RP
<i>E.coli</i>	AG, CU, PB, PC	CB, CI	GF, AK, GM, ZN, TE, RC, CH, CF, BA, AS, FG, CP, CU, NX, NA, ZX, RP, OX, TT
<i>Morganella morganii</i>	RC, CI, TE, PC, PB, AG, CU, OX	AK, GM, CH, CP	TT, RP, ZX, CB, NA, NX, FG, AS, BA, CF, ZN, GF
<i>C.diversus</i>	AS, BA, CF, PC, CH, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB		
<i>Pseudomonas aeruginosa</i>	TT, RP, AG, CU, FG, OX, CB, PB, ZN, AS, CF, CH, CI, TE, PC		BA, RC, GM, AK, GF, ZX, NA, NX, CP
MBL Producing uropathogens			
<i>E.coli</i> strain 1	CH	PC	AS, BA, CF, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>E.coli</i> strain 2	CH	AK	AS, BA, CF, PC, RC, CI, TE, ZN, GM, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Pseudomonas aeruginosa</i>			AS, BA, CF, PC, CH, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>E.coli</i> strain 3	RC		AS, BA, CF, PC, CH, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Klebsiella pneumonia</i> strain 1			AS, BA, CF, PC, CH, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Klebsiella pneumonia</i> strain 2	CH	AK	AS, BA, CF, PC, CH, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>C.diversus</i>	OX, BA, CH, GM	TE, AK, GF	AS, CF, PC, CH, RC, CI, ZN, GM, TT, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB

Key:

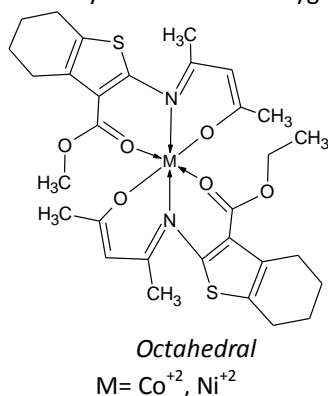
TT - Ticarcillin/clavulanic acid, OX - Oxytetracycline, RP - Ceftriaxone, ZX - Cefepime,
CB - Cefuroxime, NA - Naladixic acid, NX - Norfloxacin, AG - Amoxycillin/clavulanic acid,
CU - Cefadroxil, CP - Cefoperazone, FG - Ceftazidime, PB - Polymixin B, AS - Ampicillin,
BA - Co-trimoxazole, CF - Cefotaxime, PC - Piperacillin, CH - Chloramphenicol,
RC - Ciprofloxacin, CI - Ceftizoxime, TE - Tetracycline, ZN - Ofloxacin, GM - Gentamicin, AK - Amikacin, GF - Gatifloxacin

Table -5: Antibacterial activity of Schiff base metal complexes against drug resistant uropathogens

Isolates	Metal complexes (200µg/µl)				
	[Mn(L)Cl]	[Co(L) ₂]	[Ni(L) ₂]	[Cu(L)Cl] ₂	[Zn(L)Cl]
ESBL Producing uropathogens showing zones of inhibition in mm					
<i>E.coli</i> strain 1	-	15	12	-	13
<i>Citrobacter diversus</i> strain 1	-	-	-	-	-
<i>E.coli</i> strain 2	-	-	-	-	-
<i>Pseudomonas aeruginosa</i>	12	14	-	12	13
<i>Citrobacter diversus</i> strain 2	15	15	12	13	14
<i>Proteus vulgaris</i>	15	-	-	-	-
Non- ESBL Producing uropathogens showing zones of inhibition in mm					
<i>Proteus vulgaris</i>	25	30	-	22	-
<i>Proteus mirabilis</i>	17	18	20	37	20
<i>E.coli</i>	-	18	-	32	18
<i>Morganella morganii</i>	-	-	-	30	-
<i>C.diversus</i>	17	25	-	30	-
<i>Pseudomonas aeruginosa</i>	22	17	16	21	-
MBL Producing uropathogens showing zones of inhibition in mm					
<i>E.coli</i> strain 1	12	12	15	14	-
<i>E.coli</i> strain 2	12	14	12	13	-
<i>Pseudomonas aeruginosa</i>	-	15	12	13	14
<i>E.coli</i> strain 3	-	13	16	14	-
<i>Klebsiella pneumonia</i> strain 1	15	-	-	12	12
<i>Klebsiella pneumonia</i> strain 2	-	-	-	14	-
<i>C.diversus</i>	17	-	-	16	13

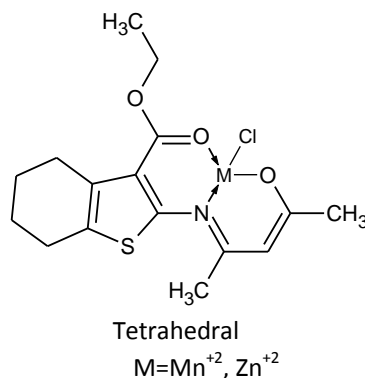
CONCLUSION

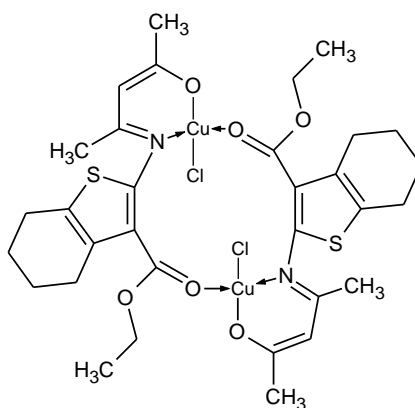
Based on the above analytical and physico-chemical properties it has been observed that a new ligand ethyl 2-[(2E, 3Z)-4-hydroxypent-3-en-2-ylidene] amino-4, 5, 6, 7-tetrahydro-1-benzothiophene-3-carboxylate behaves as a tridentate chelating agent and bonded to the metal ion through azomethine nitrogen, ester carbonyl and enolic oxygen atom.



Electronic spectra and magnetic susceptibility measurement reveal octahedral geometry for Ni (II) and Co (II) complexes, tetrahedral configuration for Mn(II) and Zn(II) complexes, and square planar dimer structure for Cu(II) complex. Structures proposed for the complexes are designated in **Figure 1-3** below.

Proposed structure of complexes





Cu (II) dimer

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