Structural investigation of some novel synthesized Schiff base Transition metal complexes derived from drug together with Antimicrobial study

Amina Mumtaz[1,2]* and Tariq Mahmud[2]
[1]PCSIR Laboratories complex, Ferozepur Road, Lahore, Pakistan
[2]Institute of Chemistry, University of the Punjab, Lahore, Pakistan

Abstract: A new series of copper (II), cobalt (II), zinc (II), nickel (II), manganese (II), iron (II) complexes with a novel Schiff base were synthesized by the condensation of sulphadizine and thiophene-2-carbaldehyde.The ligand and its complexes were characterized by using diverse instrumental procedures like microanalysis, thermo gravimetric examination and spectroscopy. The integrated ligand and its metal complexes were subjected to antibacterial studies. These studies demonstrated the enhanced activity of metal complexes against reported microbes with respect to the Schiff base.

Keywords: Schiff base, metal complex, sulphadizine, thiophene-2-carbaldehyde, antibacterial.

INTRDUCTION

Compounds derived from amines with carbonyl compounds after primary condensation are known Schiff bases (Schiff, 1864). Schiff bases are broadly utilized as bi- or tri- dentate ligands in coordination chemistry as they have capability of forming exceptionally stable transition metal complexes (Brown and Roberts, 1984; Anacona and Rincones, 2015). Schiff base and their metal complexes are significantly important in biochemical (Campos, *et al.,*1999; Anacona *et al.*, 2014; Anacona *et al.*, 2015; Chinnasamy *et al.*, 2010; Arif *et al.* 2011; Aboul-Fadl *et al.*, 2003, Ali *et al.*, 2012), analytical (Hao and Shen, 2000; Tantaru *et al.*, 2002), industrial (George *et al.*, 1993; Levitin *et al.*, 2005; Kaul *et al.*, 1986; Fakhari *et al.*,2005) and inorganic chemistry (Chakraborty *et al.*, 1994; Zhao *et al.,* 1998; Sreekala *et al.*, 1999).

The wide usage of anti-infection agents in human and animals and their wide use in areas other than the treatment and prophylaxis of sickness, have realized a noteworthy issue of medicine resistance. More bacterial strains have ended up impervious to the accessible medications. Different methodologies have been worked out and attempted upon to adapt to the resistance issue and upgrade the movement, or widen the range of the medications (Rice, 2006).

The metal complexes of Schiff bases derived from different drugs are proved as good antibacterial agents. So the present work has endeavored to broaden the extent of derivatization by giving more adaptability through Schiff base ligand. Here we report preparation, characterization and biological studies of a novel Schiff base obtained by condensation of sulphadizine and thiophene-2-carbaldehyde and its complexes with transition metal ions.

MATERIALS AND METHODS

General

All the reagents used were Analar grade (Alfa Aesar). Sulphadizine and thiophene-2-carbaldehyde were taken from BDH. Solvents (99.9%) were purchased from Alfa Aesar and were used without further purification.

Microanalysis was performed utilizing normal strategies. Transition metals in the complexes were assessed by atomic absorption spectroscopy. Carbon, hydrogen and nitrogen were estimated using CE-440 Elemental analyzer, FT-IR spectra were recorded with a Perkin Elmer Spectrum-100 spectrometer utilizing KBr pallets. NMR spectra were taken on a JEOL ECS 400 spectrometer. Mass spectra were measured with the assistance of Thermo Scientific Exactive TM Plus Orbitrap spectrometer. Thermo gravimetric analyses (TGA) for metal complexes were completed on a SDT-Q600 instrument. Magnetic moments were estimated using Evans balance with anhydrous calcium chloride. Electronic absorption spectra of all the complexes were recorded on a Shimadzu-1800 spectrophotometer. Jenway-4510 was employed to measure the conductance of Schiff base and its metal complexes in DMSO.

Preparation of Schiff base

Sulphadizine (2.0 mmole) was dissolved in 1M sodium hydroxide solution. To this, ethanolic solution of thiophene-2-carbaldehyde (2.0 mmole) was added and refluxed for one hour. A turbid white solution was collected for isolation of Schiff base ligand by

**Corresponding author:* e-mail: amina.mumtaz@hotmail.com

crystallization. The crystalline product was dried under vacuum and kept in a desiccator for further use. Thin layer chromatography (TLC) confirmed the purity of product.

Preparation of Schiff base metal complexes

2.0 mmole of ligand (L) in 10ml ethanol and 1.0 mmole chloride salts of transition metal [copper (II), cobalt (II), zinc (II), nickel (II), manganese (II), iron (II)] were dissolved in 10 ml ethanol separately and then mix. The reaction mixture was refluxed for 2h. After preparation, the coloured precipitate of Schiff base metal complexes were filtered off, washed with water, ethyl alcohol and dried under reduced pressure at room temperature.

Antimicrobial assay

In vitro antimicrobial tests were estimated by agar well diffusion method (Aulton, 2007). The antimicrobial activities of synthesized compounds were investigated against Escherichia coli, Enterobacter aerogenes, Staphylococcus aureus, Bacillus pumilus, Klebsiella oxytoca and Clostridium butyrium.

RESULTS

The synthesis of ligand was accomplished by refluxing the drug and aldehyde in a molar ratio 1:1 in ethanol. The metal complexes of the synthesized ligand were prepared using respective metal chloride and the ligand in a 1:2 molar ratio. All the metal complexes were amorphous solids and have different decomposition points. They are insoluble in water, organic solvents, partially soluble in acetone and completely soluble in DMF and DMSO. The characterization was done with Elemental analyzer FT-IR, NMR, Mass spectroscopy, TGA and micro-analytical data. The structure of synthesized Schiff base ligand along with metal complexes were investigated by different techniques and characterized as follows:

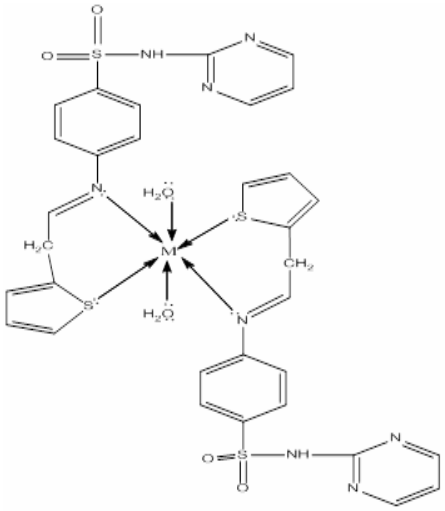

Fig. 1: Proposed structure of Schiff base metal complexes [M = Cu (II), Co (II), Zn (II), Ni (II), Mn (II), Fe (II)]

Schiff base ligand: [*N*-4-(thiophene-2-yl methyleneamino pyrimidin-2-yl-benzene sulfonamide].

Yield 65%, Color (White). m. p. 166-168^{o}C. IR (KBr, cm^{-1}) 3294 (NH), 1620 (HC=N azomethine), 1581 (C=N-pyrimidine), 1177 (O=S=O), 1087 (C-N). Anal. Calcd. For $C_{15}H_{12}N_4O_2S_2$ (367); Calcd: C, 52.26; H 3.48; N, 16.25; Found: C, 52.18; H 3.32; N, 16.34 %.

^{1}H NMR (DMSO-D_6, δ ppm) 8.74 (-CH=N), 6.34-7.78 (phenyl); ^{1}C NMR (DMSO-D_6, δ ppm) 163.3 (-CH=N), 157.5-158.7(pyrimadine), 122.3-147.5 (phenyl). MS (EI); m/z (%) = 367.0288 [M + Na].

Copper (II) complex of ligand

Yield 70%, Color (Green). decomp. p. >300 ^{o}C. IR (KBr, cm^{-1}) 3255 (NH), 1622 (HC=N azomethine), 1581 (C=N-pyrimidine), 1126 (O=S=O), 493 (M-N), 347 (M-O). UV (DMSO) λ_{max} (cm^{-1}) 15350, 23255; B.M (1.94 μ_{eff}); molar conductance (32μS cm^{-1}). Anal. Calcd. For $C_{30}H_{24}N_8O_4S_4Cu$ (788.40); Calcd: C, 45.66; H 3.04; N, 14.20; Cu, 8.06 Found: C, 45.70; H 3.01; N, 14.50; Cu, 7.97%.

Cobalt (II) complex of ligand

Yield 72%, Color (Pink). decomp. p.>300^{o}C. IR (KBr, cm^{-1}) 3255 (HN), 1627 (HC=N azomethine), 1573 (C=N-pyrimidine), 1149 (O=S=O), 493 (M-N), 363 (M-O).

UV (DMSO) λ_{max} (cm^{-1}) 17710, 21782; B.M (4.92μ_{eff}); molar conductance (55 μScm^{-1}). Anal. Calcd. For $C_{30}H_{24}N_8O_4S_4Co$(783.79); Calcd: C,45.93; H, 3.06; N, 14.28; Co, 7.51 Found: C, 45.82; H 3.57; N, 14.40; Co, 6.52%.

Zinc (II) Complex of ligand

Yield 71%, Color (Off white). decomp. p.>300^{o}C. IR (KBr, cm^{-1}) 3255 (HN), 1624 (HC=N azomethine), 1573 (C=N- pyrimidine), 1149 (O=S=O), 501 (M-N), 345 (M-O).

UV (DMSO) λ_{max} (cm^{-1}) 28420; Diamagnetic; molar conductance (13 μS cm^{-1}). Anal. Calcd. For $C_{30}H_{24}N_8O_4S_4Zn$ (790.24); Calcd: C, 45.55; H 3.03; N, 14.16; Zn, 8.27 Found: C, 45.49; H, 3.17; N, 14.29; Zn, 8.21%.

Nickle (II) Complex of Ligand

Yield 71%, Color (Bluish Green). decomp. p.>300^{o}C. IR (KBr, cm^{-1}) 3255 (HN), 1623 (HC=N azomethine), 1573 (C=N- pyrimidine), 1141 (O=S=O), 501 (M-N), 347 (M-O). UV (DMSO) λ_{max} (cm^{-1}) 16535, 24345; B.M (2.95μ_{eff}); molar conductance (51 μS cm^{-1}). Anal. Calcd. For $C_{30}H_{24}N_8O_4S_4Ni$ (803.49); Calcd: C, 45.94; H 3.06; N.

Manganese (II) Complex of Ligand

Yield 71%, Color (Off white). decomp. p. >300^{o}C. IR (KBr, cm^{-1}) 3255 (NH), 1625 (HC=N azomethene), 1573

Table 1: Thermal analysis data of the metal (II) complexes

S. NO.	Metal Chelate	Temperature Range(^{0}C)	Mass Loss % Found (Calculated)	Assignment
1.	$[Cu(L\text{-}H)_2(H_2O)_2]$	153-233 233-395	5.13(4.56) 35.55(36.55)	Loss of $2H_2O$ Loss of 2-imino-pyrimidine + Loss of $2SO_2$
2.	$[Co(L\text{-}H)_2(H_2O)_2]$	135-231 231-407	5.29(4.59) 37.00(36.77)	Loss of $2H_2O$ Loss of 2-imino-pyrimidine + Loss of $2SO_2$
3.	$[Zn(L\text{-}H)_2(H_2O)_2]$	134-230 230-405	4.89(4.55) 37.22(36.46)	Loss of $2H_2O$ Loss of 2-imino-pyrimidine + Loss of $2SO_2$
4.	$[Ni(L\text{-}H)_2(H_2O)_2]$	140-238 238-399	5.29(4.59) 37.33(36.77)	Loss of $2H_2O$ Loss of 2-imino-pyrimidine + Loss of $2SO_2$
5.	$[Mn(L\text{-}H)_2(H_2O)_2]$	150-239 239-405	4.88(4.61) 37.68(36.95)	Loss of $2H_2O$ Loss of 2-imino-pyrimidine + Loss of $2SO_2$
6.	$[Fe(L\text{-}H)_2(H_2O)_2]$	145-240 240-398	5.11(4.61) 37.77(36.91)	Loss of $2H_2O$ Loss of 2-imino-pyrimidine + Loss of $2SO_2$

Table 2: Antibacterial activity of Schiff base ligand and their metal complexes (zone of inhibition; 400µg mL-^{1})

Compound	*E. coli*	*E. aerogenes*	*S. aureus*	*B. pumilus*	*K. oxytoca*	*C. butyrium*
$[Cu(L)_2(H_2O)_2]$	29	19	30	18	18	26
$[Co(L)_2(H_2O)_2]$	27	18	25	14	15	23
$[Zn(L)_2(H_2O)_2]$	24	17	27	19	18	26
$[Ni(L)_2(H_2O)_2]$	20	12	31	18	14	22
$[Mn(L)_2(H_2O)_2]$	26	13	24	21	16	28
$[Fe(L)_2(H_2O)_2]$	22	12	22	20	14	24
Ligand	14	10	15	10	11	15
Drug	11	7	12	8	7	9

(C=N- pyrimidine), 1149 (O=S=O), 493 (M-N), 362 (M-O). UV (DMSO) λ_{max} (cm^{-1}) 16507, 25786; B.M (5.61μ_{eff}); molar conductance (56 µS cm^{-1}). Anal. Calcd. For $C_{30}H_{24}N_8O_4S_4Mn$ (779.79); Calcd: C,46.65; H 3.07; N, 14.36; Mn, 7.04 Found: C, 46.83; H 3.61; N,14.48; Mn, 6.94%.

Iron (II) complex of ligand

Yield 73%, Color (Orange). decomp. p. >300**º**C. IR (KBr, cm^{-1}) 3255 (HN), 1623 (HC=N azomethine), 1573 (C=N-pyrimidine), 1149 (O=S=O), 501 (M-N), 324 (M-O).

UV (DMSO) λ_{max} (cm^{-1}) 28409, 30211; B.M (5.37μ_{eff}); molar conductance (41 µS cm^{-1}). Anal. Calcd. For $C_{30}H_{24}N_8O_4S_4Fe$ (780.70); Calcd: C, 46.11; H 3.07; N, 14.34; Fe, 7.15 Found: C, 46.33; H, 3.51; N, 14.45; Fe, 6.93%.

DISCUSSION

NMR spectra

^{1}H NMR and ^{13}C NMR Spectra were taken in DMSO-d_6. The peaks of all the proton and carbon atoms were fixed in their expected region. The NMR spectra of Schiff base ligand was confirmed the absence of aldehyde peak at δ 9-10 and presence of azomethine at δ 8.74. ^{13}C NMR spectra also verified azomethine peak at δ 163.3. The diamagnetic zinc (II) complex showed a slight change in spectra because of increased conjugation and coordination to metal ions.

IR spectra

The metal ligand bond was verified by comparing the IR spectra of the Schiff base ligand with its metal (II) complexes. The FT-IR spectra predicted all the absorption bands of the Schiff base ligand and the appearance of some new bands at specific wave numbers confirmed the modes of absorption and formation of the complex with the metal ions through nitrogen and oxygen. The azomethine group of ligand 1620cm^{-1} was shifted to higher value (1627cm^{-1}) in all the complexes. This suggested the coordination of metal to ligand bond through azomethine (HC=N). Absorption bands of the sulfonamides moiety in the synthesized ligands and in metal complexes have same frequency. The coordination of the Schiff-bases with the metal ions was further

confirmed by the appearance of new bands between 493-501 and 324-363cm^{-1} designate to the metal nitrogen (M-N) and metal-oxygen (M-O) extending vibrations, individually (Nakamoto, 1970; Aurora 2014). These bands were not present in the spectra of the free ligand, thus affirming the participation of O and N in the coordination with transition metal ions.

Electronic spectra and magnetic susceptibility

The electronic absorption spectra of transition metal (II) complexes were recorded in 10^{-3}M solutions of each complex in DMSO in the range 2000-10000cm^{-1} at room temperature.

The electronic spectrum of Mn (II) and Fe (II) complexes shows $^6A_{1g} \rightarrow {}^4A_{1g}(G)$, $^6A_{1g} \rightarrow {}^4A_{1g}\ 4E_g$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ and $^5T_{2g} \rightarrow {}^5E_g$ transitions respectively. The magnetic moment values of complexes supports octahedral geometry i.e. 5.61 B.M and 5.37 B.M.

The electronic absorption spectrum of the Cu II) complex showed two bands at 15350cm^{-1} and 23255cm^{-1} corresponding to the transition $^2B_{1g} \rightarrow {}^2A_{1g}$. No spectral bands were found below 10000cm^{-1} which supports octahedral geometry. Also, the magnetic moment value (1.94 B.M) for the Cu (II) complexes suggests the octahedral geometry with d_{x2-y2} ground state.

The spectrum of the Ni (II) complex showed d-d bands in the region 16535 and 24, 345cm^{-1} showed the spin-allowed transitions $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$, respectively with the octahedral configuration. The magnetic moment (2.95 B.M) value confirmed the presence of two unpaired electrons Ni (II) ion also consistent with an octahedral geometry for the Ni (II) complex.

The electronic spectra of Co (II) complex in DMSO exhibited bands around 17,710 cm^{-1} and a strong high-energy band at 21782 cm^{-1} designed $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions respectively, for a high-spin octahedral geometry. The magnetic susceptibility measurements (4.92 B.M) for the solid Co (II) complex are also indicative of three unpaired electrons per Co (II) ion consistent with their octahedral environment (Cotton *et al.*, 2003). The spectrum of Zn (II) complex exhibited only one band at 28,340cm^{-1} which was assigned to a ligand→metal charge transfer. The zinc (II) complex was observed as diamagnetic.

Thermal studies

Thermo gravimetric analyses (TGA) for the transition metal complexes were done from room temperature to 1000^{o}C. Calculated and observed mass losses are shown in the table below.

Antibacterial activity

All the synthesized metal complexes and Schiff base ligand were tested against *Escherichia coli, Enterobacter aerogenes, Staphylococcus aureus, Bacillus pumilus, Klebsiella oxytoca* and *Clostridium butyrium,* according to literature (Anacona *et al.*, 2014; Arif *et al.*, 2011). The results showed enhanced activity when coordinated with transition metals (table 2).

CONCLUSION

The characterization data including Electronic spectra and magnetic susceptibility revealed that all the synthesized metal complexes have octahedral geometry. The antibacterial studies showed enhanced antibacterial properties against selected microbes as compared to the ligand. These observations, in accordance with different studies, recommend that metal based drugs have potential as therapeutics.

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