Moroccan Journal of Chemistry
ISSN: 2351-812X
http://revues.imist.ma/?journal=morjchem&page=login
A. Athar / Mor. J. Chem. 4N°4 (2016) 945-953

Transition Metal Complexes of Sulfonamide Based Schiff Bases: PreparationCharacterization and Antibacterial Activity.

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Received 23 July 2016,
Revised 10 Aug 2016,
Accepted 11 Jan 2017

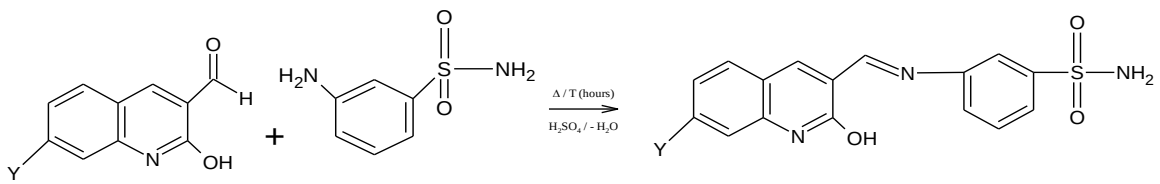
Abstract

Metal complexes of Cu (II), Co (II), Ni (II) and Zn (II) of Schiff based derived from 2-hydroxy-7-methylquinoline-3-carbaldehydeand 2-hydroxy-7-methoxyquinoline-3-carbaldehyde with 3-aminobenzenesulfonamide have been prepared and characterized on the basis of their physical characteristics, micro-analytical data, ^{1}H NMR, FTIR and UV spectrum data. The spectrum data confirmed coordination of Schiff base with metal through imine nitrogen and oxygen atom. While electronic spectrum data confirmed the octahedral geometry of the complexes. Biological screening effect of Schiff base and their metal complexes have been studied against gram positive and gram negative bacteria by disc diffusion technique. Biological activities show that the complexes exhibit higher antibacterial activity than that of Schiff base against tested bacteria.

Keywords: NO donor Schiff base, transition metal complexes, micro-analytical data, spectral characterization, biological activity

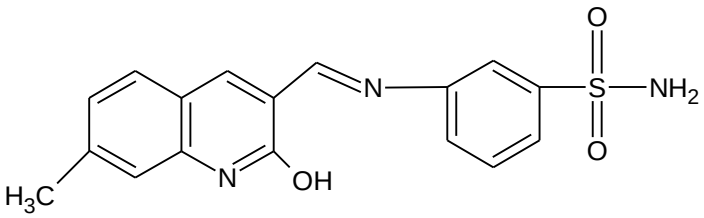
1. Introduction

Schiff bases derived from amino group and carbonyl group of an aldehyde are an important class of ligand which coordinated with transition metal ions via azomethine nitrogen and have been studied extensively [1]. Schiff base ligands and their metal complexes have expended enormously and included vast area of organometallic compounds and various aspects of bioinorganic chemistry. The coordination chemistry of Schiff base as bidentate ligand are gaining much importance due to their biological and industrial applications [2, 3]. Sulfonamides compounds were the first drug found to act selectively and used as preventative and therapeutic agent against various diseases. The presence of sulfonamide functional group is responsible for antimicrobial activity, which can be altered depending upon the type of substituent present on the aromatic rings. [4, 5]. Schiff bases derived from sulfa drugs acquired interest due to their useful application in biological system. The condensation product of sulfa drugs with aldehydes and ketones are biologically active and also have good complexing, their activities increases thecomplexation with metal ions [6]. Schiff base ligands have been reported to show different variety of biological actions because of their –C=N (azomethine linkage) group which responsible for antibacterial, antifungal, clinical and analytical activities [7]. Transition metal complexes with oxygen and nitrogen donor Schiff bases are of particular interest because of their abilities to possess unusual configuration [8]. In the present research work, Schiff bases 3-{[(1*E*)-(2-hydroxy-7-methylquinolin-3-yl)methylene]amino}benzenesulfonamideand 3-{[(1*E*)-(2-hydroxy-7-methoxyquinolin-3-yl)methylene]amino}benzenesulfonamidewere prepared by refluxing 2-hydroxy-7-methylquinoline-3-carbaldehydeand 2-hydroxy-7-methoxyquinoline-3-carbaldehydewith 3-aminobenzenesulfonamide and their metal complexes were synthesized with Cu (II), Co (II), Ni (II) and Zn (II). Structure of the ligand and metal complexes were characterized by FTIR, ^{1}H NMR and UV spectroscopy. Biological activities were also studied against gram-positive and gram-negative bacteria for ligand and metal complexes. Structure of the Schiff base ligand synthesized in present work is shown in scheme 1.

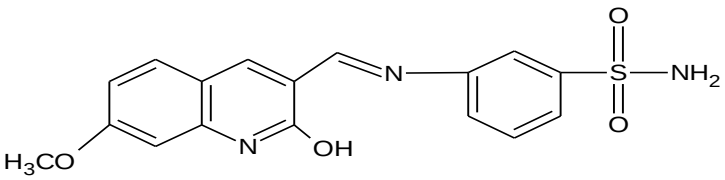


Where Y = -CH_3 and -OCH_3

Scheme I. Preparation of Ligand



HL^{1}



HL^{2}

Scheme II. Structures of Ligands (HL^{1} and HL^{2})

II. Material and Instruments

All the chemical reagents used were of analytical grade and of the highest purity available and were used without further purification. 3-aminobenzenesulfonamide were obtained from E.Merck. 2-hydroxy-7-methylquinoline-3-carbaldehyde and 2-hydroxy-7-methoxyquinoline-3-carbaldehydeobtained from Health Chemicals Co. Ltd.and Metal (II) acetate salts were obtained from Sigma-Aldrich. Solvents used were distilled and purified before used, these are obtained from Fluka and Sigma-Aldrich. Melting point of the ligands and of the transition metal complexes were determined in capillary tube using melting point apparatus. Infrared spectra were measured as KBr pellets on FT-IR spectrometer Shimadzu Japan Model IR Prestige-21 in the frequency range 4000-400 cm^{-1}. The electronic spectra were measured using DMSO as a solvent on U.V.Spectrophotometer Shimadzu Japan model Pharmaspec-1700. ^{1}H-NMR spectrum of the ligands and of their transition metal complexes were recorded using NMR-spectrometer Bruker Germany 300MHz. The elemental analysis was performed on Elemental Analyzer Leco USA model CHNS-932.

2.1 Synthesis

Ligands were synthesized by the reported method and transition metal complexes of Schiff bases were prepared by mixing the corresponding ligands with transition metal acetates i.e $Cu(CH_3COO)_2.2H_2O$, $Co(CH_3COO)_2.2H_2O$, $Ni(CH_3COO)_2.2H_2O$ And $Zn(CH_3COO)_2.2H_2O$.

2.2 Synthesis of Schiff base ligand

Solution of sulfonamide of pre-determined concentration was added to the solution of aldehyde of known concentration in ethanol and then few drops of conc. H_2SO_4were added to the reaction mixture which was heated under reflux for a fixed period of time at constant temperature. The product obtained was washed and recrystallized to obtain precipitation of the ligand. [9].

a. 3-{[(1*E*)-(2-hydroxy-7-methylquinolin-3-yl)methylene]amino}benzenesulfonamide:(HL^1)

0.1M solution of 3-aminobenzenesulfonamide (25 ml) was added to 0.1M solution of 2-hydroxy-7-methylquinoline-3-carbaldehyde (25 ml) in ethanol and then few drops of conc. Sulfuric acid (H_2SO_4) wereadded to the reaction mixture, and mixture was heated under reflux for about 5 hours at 75^{o}C. The solutionso obtained was further concentrated by adding distilled water on water bath. The product obtained was precipitated, cooled and collected after filtration. The precipitate was purified by washing with distilled water and then with petroleum ether. The product was again recrystallized in ethanol and dried in vacuum dessicator overnight. After completion of the reaction process precipitate (ppt) of the ligand were formed out as colored solids. Purity of the ligand was checked by M. P. and TLC. The ligand was soluble in methanol, ethanol, Dimrthylformamide (DMF) andDimethly sulfoxide(DMSO).

b. 3-{[(1*E*)-(2-hydroxy-7-methoxyquinolin-3-yl)methylene]amino}benzenesulfonamide:(HL^2)

0.1M solution of 3-amiobenzenesulfonamide (25 ml) was added to 0.1M solution of 2-hydroxy-7-methoxyquinoline-3-carbaldehyde (25 ml) in ethanol than few drops of conc. Sulfuric acid (H_2SO_4)were added to the reaction mixtureand reaction mixture was heated under reflux for about 6 hours at 70^{o}C. The solution so obtained was further concentrated by adding distilled water on water bath. The product obtained was precipitated, cooled and collected after filtration. The precipitate was purified by washing with distilled water and then with petroleum ether. The product again recrystallized in ethanol. The product was again recrystallized in ethanol and dried in vacuum desiccator overnight. After completion of the reaction process precipitate of the ligand were obtained as colored solids. Purity of ligand was checked by M. P. and TLC. The ligand was soluble in methanol, ethanol, DMF and DMSO.

2.3 Synthesis of Metal complexes

Metal complexes of the Schiff base ligand were prepared by mixing 0.2M of HL^1 and HL^2 Schiff bases (25 ml) with 0.1M of Cu, Co, Ni and Zn salts (25 ml) keeping ligand-metal ratio 2:1 in ethanol. The resultant solution mixture was than refluxed for 5-7 hours at 70°C-75°C where solid colored complexes precipitate were obtained. The complex obtained in each time was cooled, filtered and washed with the ethanol many times to purify and remove the excess of ligand. Finally complexes were placed in desiccators for drying. [10]

III. RESULT AND DISCUSSION

Schiff base were synthesized by treat equimolar quantities of 3-aminobenzenesulfonamide with 2-hydroxy-7-methylquinoline-3-carbaldehyde and 2-hydroxy-7-methoxyquinoline-3-carbaldehyde. These Schiff baseson mixing with transition metal acetate then formed Schiff base transition metal complexes. Metal complexes so obtained were found stable at normal temperature and were colored solids. Physical characteristics and analytical data of ligands and metal complexes are given in table 1 and table 2.

TABLE 1: Physical characteristics of Schiff base and their metal complexes

Sr. No.	Ligand/ Complexes	Color	Molecular Formula	Molecular Mass($gmol^{-1}$)	M. P. (°C)	Yield (%)
1	HL^1	Pale Yellow	$C_{17}H_{15}N_3O_3S$	341.38	178	80
2	$Co(HL^1)$	Dark green	$C_{34}H_{30}N_6O_6S_2Co.2H_2O$	777.69	188	82
3	$Ni(HL^1)$	Light green	$C_{34}H_{30}N_6O_6S_2Ni.2H_2O$	777.45	190	79
4	$Cu(HL^1)$	Yellowish green	$C_{34}H_{30}N_6O_6S_2Cu.2H_2O$	782.31	185	81
5	$Zn(HL^1)$	Dark orange	$C_{34}H_{30}N_6O_6S_2Zn.2H_2O$	784.15	198	80
6	HL^2	Dark Brown	$C_{17}H_{15}N_3O_4S$	357.38	180	83
7	$Co(HL^2)$	Yellow Brown	$C_{34}H_{30}N_6O_8S_2Co.2H_2O$	809.69	175	82
8	$Ni(HL^2)$	Light Brown	$C_{34}H_{30}N_6O_8S_2Ni.2H_2O$	809.45	192	78
9	$Cu(HL^2)$	Brown	$C_{34}H_{30}N_6O_8S_2Cu.2H_2O$	814.31	182	77
10	$Zn(HL^2)$	Light yellow	$C_{34}H_{30}N_6O_8S_2Zn.2H_2O$	816.15	195	79

TABLE 2: Micro-analytical data of Schiff base and their metal complexes

Sr. No.	Ligand/ Complexes	Elemental analysis (%). *(calculated)/ found*					Metal (%) *(calculated)/ found*
		C	H	N-$	O	S	
1	HL^1	(59.81)	(4.43)	(12.31)	(14.06)	(9.39)	--
		59.78	4.30	12.19	13.94	9.25	--
2	$Co(HL^1)$	(52.46)	(3.86)	(10.80)	(12.34)	(8.23)	(7.58)
		52.31	3.72	10.67	12.20	8.10	7.44
3	$Ni(HL^1)$	(52.48)	(3.86)	(10.80)	(12.35)	(8.23)	(7.55)
		52.34	3.74	10.66	12.22	8.11	7.42
4	$Cu(HL^1)$	(52.15)	(3.83)	(10.74)	(12.27)	(8.18)	(8.13)
		52.01	3.70	10.63	12.13	8.14	8.00
5	$Zn(HL^1)$	(52.03)	(3.82)	(10.71)	(12.24)	(8.16)	(8.34)
		51.90	3.71	10.68	12.10	8.02	8.20
6	HL^2	(57.13)	(4.23)	(11.76)	(17.91)	(8.87)	--
		57.00	4.10	11.64	17.80	8.73	--
7	$Co(HL^2)$	(50.39)	(3.70)	(10.37)	(11.86)	(7.90)	(7.28)
		50.24	3.68	10.23	11.72	7.78	7.15
8	$Ni(HL^2)$	(50.40)	(3.71)	(10.38)	(11.86)	(7.91)	(7.28)
		50.28	3.59	10.25	11.72	7.79	7.15
9	$Cu(HL^2)$	(50.10)	(3.68)	(10.31)	(11.79)	(7.86)	(7.80)
		49.98	3.55	10.19	11.68	7.76	7.77
10	$Zn(HL^2)$	(50.00)	(3.67)	(10.29)	(11.76)	(7.84)	(8.01)
		49.89	3.56	10.15	11.67	7.70	7.90

3.1 Infrared Spectroscopy

Structure of the Schiff base metal complexes was established with the help of infrared spectroscopy. IR spectra of the free ligand and its metal complexes were recorded using KBr pellets in the range 4000-400 cm^{-1}. The infrared spectral data of the Schiff base ligand and its metal complexes are listed in table 3. Bands observed for ligand HL^1 at 3324 cm^{-1} and for ligand HL^2 at 3310 cm^{-1} are due to H-N linkage which is shifted to higher frequency when the ligand form complexes with metals. Sharp bands observed for ligand HL^1 at 1582 cm^{-1} and for ligand HL^2 at 1590 cm^{-1} are due to azomethine>C=N linkage which is shifted to higher frequency whileformingmetal complexes due to coordination of the azomethine linkage with metal ion [11,12]. The presence of $-SO_2$ groupin Schiff bases (HL^1 and HL^2) is confirmed by appearance of two bands at 1155 cm^{-1} and 1325 cm^{-1} and at 1134 cm^{-1} and 1344 cm^{-1} respectively due to symmetric and asymmetric vibrations. These bands remain at the same positions in case of ligand while the complexes indicate that oxygen of $–SO_2$ group is not coordinated with the metal ion [13]. The strong bands of ligand HL^1 at 3372 cm^{-1} and of ligand HL^2 at 3384 cm^{-1} due to >O-H group in ligand were shifted to lower frequency on chelating with metal ion indicating the O-H group can act as coordinating site in both ligands [14]. The coordination of nitrogen of azomethine further supported by non-ligand band >M-N which appears in the region 498-470 $cm^{-1}$and >M-O appears in region of

550-578 cm^{-1}in all complexes of both ligands HL^1 and HL^2 [15]. All the metal complexes of Schiff base show bands in the region of 1490-1534 cm^{-1} which indicates the presence of coordinated water molecules with the metal ion [16].

TABLE 3: IR spectra cm^{-1} of Schiff base and its metal complexes

Compound	N-H	C=N	SO_2		O-H	M-O	M-N	H_2O
			Sym.	**Asym.**				
HL^1	3324	1582	1325	1155	3372	--	--	--
Cu HL^1	3286	1608	1320	1153	3396	578	470	1490
Co HL^1	3274	1620	1324	1152	3414	567	474	1510
NiHL^1	3268	1618	1323	1154	3420	540	480	1505
Zn HL^1	3280	1624	1322	1150	3408	554	466	1514
HL^2	3310	1590	1344	1134	3384	--	--	--
Cu HL^2	3266	1602	1345	1135	3398	550	486	1498
Co HL^2	3245	1625	1342	1138	3412	548	492	1512
NiHL^2	3270	1616	1348	1133	3424	562	484	1522
Zn HL^2	3254	1610	1346	1132	3442	552	498	1534

3.2.Electronic Spectra

Electronic spectra of the ligands and its metal complexes have been displayed in Dimethylformamide (DMF) solution. Electronic spectra of the ligand HL^1 shows absorption in UV/ visible region two high intensity bands at 32573 $cm^{-1}$and 29325 cm^{-1}which indicate n → n* and л →л* transition of azomethine group in the ligand [17]. The electronic spectra of Cu (II) complex shows two energy bands at 20243 cm^{-1} and 16163 cm^{-1}. This is due to $^4T_{2g}$ (F) → $^4A_{2g}$(F) and $^4T_{1g}$ (F) → $^4T_{2g}$(P) transition respectively, which indicates presence of octahedral geometry around Cu (II) [18]. The electronic spectra of Co (II) complex shows three energy bands at 35852 cm^{-1} and 31653cm^{-1} due to $^2B_{1g}$ → $^2A_{1g}$and $^2B_{1g}$ → $^2B_{2g}$. The electronic spectra of Co (II) complex suggests an octahedral geometry [19]. The electronic spectra of Ni (II) shows absorption band at 24962 cm^{-1} and 19927 cm^{-1}assigned to $^3A_{2g}$ (F) → $^3T_{1g}$(F) and $^3A_{2g}$(F) → $^3T_{1g}$(P) transitions, indicating octahedral geometry of Ni (II) complex[20]. The Zn (II) complex shows high energy band at 33437 cm^{-1} and 23,455 cm^{-1}due to ligand → metal charge transfer [21]. Similarly electronic spectra of ligand HL^2shows absorption two high intensity bands at 38272 $cm^{-1}$and 32550 cm^{-1} indicating n → n* and л →л* transition of azomethine group in the ligand . The electronic spectra of Cu (II) complex shows two energy bands at 33075 cm^{-1} and 25873 cm^{-1}due to $^4T_{2g}$ (F) → $^4A_{2g}$ (F) and $^4T_{1g}$ (F) → $^4T_{2g}$ (P)transition respectively indicating an octahedral geometry around Cu (II). The electronic spectra of Co (II) complex shows three energy bands at 33075 cm^{-1} and 25873 cm^{-1} due to $^2B_{1g}$ → $^2A_{1g}$and $^2B_{1g}$ → $^2B_{2g}$. This band is assigned to metal-ligand charge transfer. The Ni (II) shows absorption band at 36794 $cm^{-1}$and 25652 $cm^{-13}A_{2g}$ (F) → $^3T_{1g}$(P) and $^3A_{2g}$(F) → $^3T_{1g}$(F) transition. The Zn (II) complex shows high energy bands at 36345 cm^{-1} and 30520 cm^{-1}due to ligand → metal charge transfer and this band are attributed tothe ligand to metal charge transfer (MLCT) as the electronic configuration of these complexes confirmed the absence of any d-d transition.

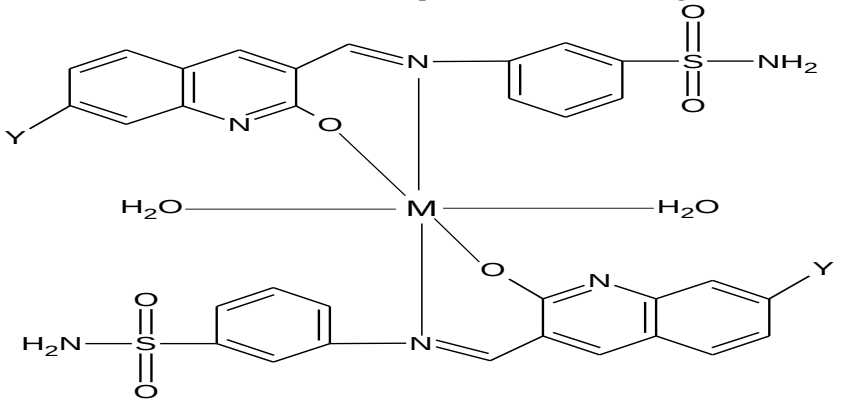
TABLE 4: Electronic spectral data of complexes

Ligand/ Complex	Wave number (cm^{-1})	Band Assignments
HL^1	32573 cm^{-1}, 29325 cm^{-1}	n → n*, л →л* transition
Cu HL^1	20243 cm^{-1}, 16163 cm^{-1}	$^4T_{2g}$ (F) → $^4A_{2g}$ (F)$^4T_{1g}$ (F) → $^4T_{2g}$(P)
Co HL^1	35852 cm^{-1}, 31653cm^{-1}	$^2B_{1g}$ → $^2A_{1g}$ $^2B_{1g}$ → $^2B_{2g}$
NiHL^1	24962 cm^{-1}, 19927 cm^{-1}	$^3A_{2g}$ (F) → $^3T_{1g}$(F) $^3A_{2g}$(F) → $^3T_{1g}$(P)
Zn HL^1	33437 cm^{-1}, 23,455 cm^{-1}	ligand → metal charge transfer
HL^2	38272 cm^{-1}, 32550 cm^{-1}	n → n*, л →л* transition
Cu HL^2	33075 cm^{-1}, 25873 cm^{-1}	$^4T_{2g}$ (F) → $^4A_{2g}$ (F) $^4T_{1g}$ (F) → $^4T_{2g}$ (P)
Co HL^2	33075 cm^{-1}, 25873 cm^{-1}	$^2B_{1g}$ → $^2A_{1g}$ $^2B_{1g}$ → $^2B_{2g}$
NiHL^2	36794 cm^{-1}, 25652 cm^{-1}	$^3A_{2g}$ (F) → $^3T_{1g}$(P) $^3A_{2g}$(F) → $^3T_{1g}$(F)
Zn HL^2	36345 cm^{-1}, 30520 cm^{-1}	ligand → metal charge transfer

^{1}H NMR Spectra

^{1}H NMR Spectra of Schiff base and its complexes have been recorded in Dimethyl sulfoxide (DMSO) solution and Tetramethylsilane (TMS) used as internal standard. In both the ligands (HL^1 and HL^2) azomethine proton appears at 8.82 ppm, but it is shifted to downfield in metal complexes which confirms coordination of ligand with metal by azomethine nitrogen [22]. The aromatic proton in Schiff base of HL^1 appears at 7.14 ppm to 8.14 ppm and in their metal complex in the range of 7.04 ppm to 8.00 ppm and in Schiff base of HL^2 appears at 6.80 ppm to 8.14 ppm and in their metal complex in the range of 6.70 ppm to 8.00 ppm [23]. In addition, the multiple signals in the range of approximately 2.48ppm and 3.87 ppm respectively for HL^1 and HL^2 are attributed to aliphatic protons. [24].

On the basis of above given data structure of the metal complex of Schiff base is given in scheme. 2



Scheme.2. Structure of transition metal complexes. Where Y = -CH_3 and -$OCH_3$and M = Cu (II), Co (II), Ni (II), Zn (II)

3.3. Antibacterial activity

Antibacterial activities of the benzenesulfonamide, its ligands and its metal complexes were determined and screened on gram positive bacteria: *S.pneumoniae* and *B. cereus* and gram negative bacteria: *K. pneumoniae* and *E. Coli* by disc diffusion technique [25]. Nutrient agar was used for the medium of bacterial growth. Nutrient agar is popular because it can grow variety types of bacteria and fungi and contains many nutrients needed for the bacterial growth. Nutrient agar, cotton swab, petri dishes and metallic borer were autoclaved for sterilization at 120^{o}C for 30 minutes. Bore of 6 mm diameter was prepared with the help of metallic borer. After solidification of the nutrient agar bacterial stain spread over the surface of the agar with the help of cotton swab.Benzenesulfonamide, its ligands and their metal complexes were dissolved in DEMSO. The sample of 1 mg/ml in DEMSO was added in the discs. Sulfonamide itself and Ciprofloxacin were taken as reference antibacterial drugs. Filter paper disc were used for the incubation period of 48 hours at 25-30^{o}C and the results were recorded. The antibacterial activities of the ligand and its complexes were tested by measuring inhibition zone observed around the material. Ligand showed significant range of activities on the growth of all the selected bacterial stain. The results suggested that complexes increased the antibacterial activity [26]. The antibacterial activity data has been presented in table 5.

TABLE 5: Antibacterial activities of ligand and its complexes (inhibition zone in mm)

Compound	**Gram +ve**		**Gram –ve**	
	S.pneumoniae	B. cereus	K. pneumoniae	E. coli
HL^{1}	13	11	15	14
Cu HL^{1}	15	14	16	16
Co HL^{1}	14	15	17	12
NiHL^{1}	16	17	18	14
Zn HL^{1}	17	16	19	15
HL^{2}	11	12	14	13
Cu HL^{2}	13	14	15	12
Co HL^{2}	14	13	17	16
NiHL^{2}	16	15	18	18
Zn HL^{2}	15	18	16	17
Sulfonamide	12	10	14	16
Ciproflocaxin	20	21	19	18

>20: significant, 15-19: modrate, < 15: weak

IV. Conclusion

New Sulfonamide based Schiff bases have been prepared by the condensation of 3-Aminochlorobenzenesulfonamide with 2-hydroxy-7-methylquinoline-3-carbaldehyde and 2-hydroxy-7-methoxyquinoline-3-carbaldehyde. The transition metal complexes prepared by reacting them with metal acetate salts. The coordination ability of the Schiff base has been reported by physical characteristics, micro-analytical data^{1}H NMR, FTIR and UV spectrum data confirm

suggested coordination of ligands, which is bidentate and linked through azomethine group and oxygen of quinoline ring forming stable chelate. The metal chelate of ligand has been structurally characterized and it has been concluded that metal complexes show coordinated octahedral geometry. Biological study shows significant activity of metal complexes as compare to that of the ligands.

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