

ELECTROSCOPIC INVESTIGATION ON STRUCTURAL CHARACTERIZATION AND MICROBIAL POTENTIAL OF NEWLY SYNTHESIZED SCHIFF BASES AND THEIR METAL COMPLEXES.

Shambuling S. Karabsannavar¹, Mallikarjun B. Kalashetti², Dr. Basavaraj M. Kalshetty^{3*},

¹Research and Development Center, Bharathiar University, Coimbatore, Tamil Nadu.

²Department of Chemistry, Karnataka University, Dharwad, Karnataka State, India.

³BLDE'S Science College, Jamkhandi District Bagalkot, Karnataka State, India.

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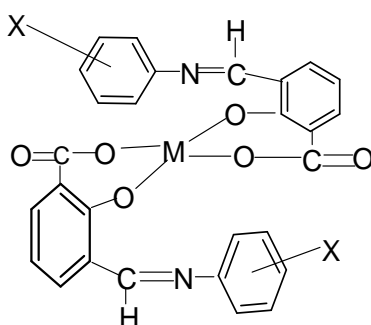
*Correspondence for
Author

Dr. Basavaraj M.
Kalshetty

BLDE'S Science College,
Jamkhandi District
Bagalkot, Karnataka State,
India.

ABSTRACT

The coordination complexes of Cu^{II}, Zn^{II}, Co^{II}, Cd^{II} and Ni^{II} with new Schiff bases derived from O-, m- and p-methoxyaniline (Anisidine) with 3 Aldehydosalicylic acid have been synthesized. The Schiff bases and organometallic complexes have been characterized on the basis of elemental analysis, IR and NMR spectra. The metal complexes were coloured and stable in air, the Schiff base ligands act as dibasic tetra dentate nature and forms 1:1 complexes with the selected metal ions (Scheme A). The Schiff bases and their metal complexes have been tested for their antimicrobial behavior against various microorganisms and all complexes showed a good activity.



Scheme - A

X = H, CH₃, OCH₃, Cl, NO₂,

KEYWORDS: Schiff base complexes, IR, NMR-spectra, dibasic 1:1 complexes, antimicrobial potential, microorganism.

INTRODUCTION

Schiff bases contain azomethine group (C=N) which is perfectly formed by the condensation of primary amines with aromatic aldehydes, are commonly bound to the metal ions.^[1-4] Such Schiff bases containing various donor atoms like O, N showed broad biological activities. The metal complexes of synthesized organic ligands played a vital role in the field of coordination Chemistry. The citation of Schiff bases towards the central metal ions enriches the study of stability and versatility of the Organometallic complexes making a greater choice of flexibility. The microbial potential of these compounds have been remarkable application and attention.^[5,7] The synthesized novel ligands were derived by the condensation of 3-Aldehydosalicylic acid with o- Anisidine, m- Anisidine and p-Anisidine in alcoholic medium. The characterization of Schiff bases and their metal complexes were evaluated for their antimicrobial in vitro-activity against several bacterial strains.^[8-10] The metal complexes of Schiff bases showed biological activities including antifungal, anticancer, anti-inflammatory, antitumor, anti convulsant, anti diabetic and herbicidal.

The Schiff base metal complexes and derivatives of Indole, triazole, Coumarin with 3-Aldehydosalicylic acid so far reported as cytotoxic drugs, anti HIV, anti tubercular and effective therapies.^[11-14] The metal complexes are still a major line of approach to develop new drugs. However, analogous of hetro- aromatic Schiff bases derived from 3-Aldehydosalicylic acid have been investigated. So thoroughly the synthesized Schiff bases and metal complexes have been to possess biological activities. The present developments of above Schiff bases and metal complexes are more fascinating. The continuation of work on the synthesis of Schiff bases of o-, m-, p-Anisidine derived from 3-Aldehydosalicylic acid on condensation and its metal complexes with different metal ions at various reaction conditions were carried out followed b standard procedures.^[15] In the recent years, metal based drugs have gained much importance in medical field.^[16,17] and the form stable complexes with metal ions due to the presence of carboxylic and a phenolic hydroxyl groups. It is predicted that the coordination behavior of Schiff base ligand would e developed on different reaction conditions (pH ranges) and are markedly different from these compounds.^[18] Hence, the synthesized Schiff bases and metal complexes were evaluated for their in-vitro ant-micro-bacterial activities against several bacterial strains.^[19]

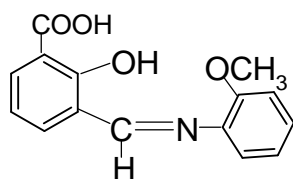
EXPERIMENTAL

Materials and methods

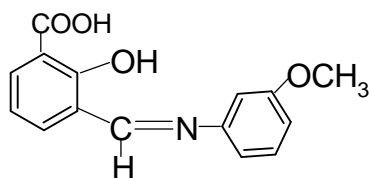
All the chemicals such as metal chlorides, sodium acetate and other solvents used were of Glaxo and Merck grade, the solvents were purified and used. The newly synthesized Schiff bases and metal complexes were prepared by standard methods.^[20, 21]

Synthesis of Schiff base ligands

A solution of *o*-Anisidine in ethanol (50ml) was prepared in a 100ml round bottomed flask fitted with reflux condenser. Then equimolar quantity of 3-Aldehydosalicylic acid was added to this solution. The resultant mixture was refluxed at 75°C to 2 hours, the reaction mixture was cooled to room temperature as a result a crystalline dark yellow compound was separated (Scheme 1), filtered and dried and purified by crystallizing in appropriate solvent.

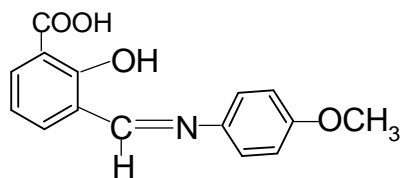


Scheme - 1



Scheme - 2

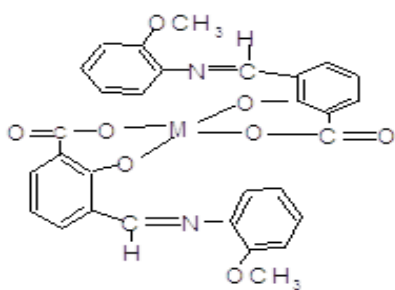
The same experimental methods were followed for other Schiff bases (Scheme 2 and Scheme 3) were synthesized by *m*-Anisidine and *p*-Anisidine by the condensation with equimolar quantity of parent ligand (3-Aldehydosalicylic acid) separately in alcoholic medium by reflux condensation. The deep yellow crystalline compounds were separated out, were filtered, dried and recrystallized in suitable solvent. The newly synthesized compounds were confirmed by IR ¹HNMR spectra and by mass spectra, which showed the evidence for the reaction completion and formation of Schiff bases and metal complexes.



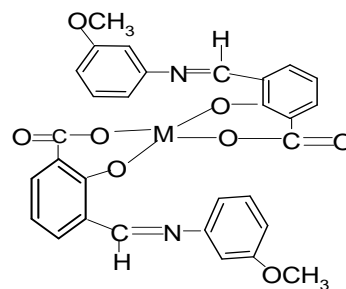
Scheme - 3

Preparation of metal complexes with Schiff base reagents

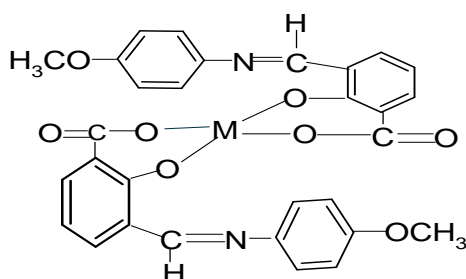
The metal complexes with the Schiff base reagents were prepared by standard reported methods. The metal salts (MX_2) were dissolved in minimum quantity of water and the solutions were added to hot ethanol solution of the corresponding Schiff bases. After complete addition little amount of sodium acetate was added and the mixture was refluxed for 2 hours, crystalline solid was obtained (Scheme 4 Scheme 5 and Scheme 6) were isolated by filtration, washed with hot water and dried in air.



Scheme - 4



Scheme - 5



Scheme - 6

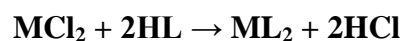
Antimicrobial activity

The biological activity of Schiff bases and their metal complexes was carried out for anti-bacterial analysis against staphylococcus aureus, Escherichia coli, Bacillus subtilis, Pseudomonas aeruginosa and aspergillus Niger for anti-fungal analysis. The bacteria and

fungi cultures were prepared; each culture was added to the sterilizer medium before solidification. The compounds were tested at 1 mg/ ml (ppm) concentration in DMSO by plate incubation method. The drug dilutions made (concentration screened) 25, 50, 100, 250, 500 and 1000 μ g serially. The test was performed at 28 $^{\circ}$ C – 29 $^{\circ}$ C and minimum inhibitory concentration (MIC) in μ g was recorded by visual observations, after 24 hours incubation. After incubation zone of inhibitions (mm) were recorded. It was observed that Schiff bases exhibited toxic behavior toward bacterial and fungal pathogens. These activities were further enhanced when the metal ions were incorporated into the Schiff base moiety. The higher activities of metal complexes may be attributed to the metal ions which has immense effect on the normal cell membrane. However, in some cases Schiff bases and their complexes with metal ions have similar activity against bacteria and fungi.^[22] Table 5 Table 6 that the metal complex compounds are more active than their respective Schiff bases. It is found that the Copper (II), complex with Schiff bases Scheme 1 and Scheme 2 showed more bio-active than other metal complexes. The higher bio-activity of Copper (II) complex may be due to the effect of copper metal ion on the normal cell processes.^[23] However, in the present investigation the biological activity increases upon metal complexation. The maximum activity was observed for copper complexes were found more toxic than Nickel complexes.

RESULT AND DISCUSSION

Light and air stable metal complexes of the general formula ML_2 have been prepared by reacting MCl_2 and HL in a 1:1 molar ratio in alcoholic medium.



The reaction mixture is refluxed for 2 hours in an alcoholic medium

The synthesized Schiff base ligands and metal complexes were highly colored and insoluble in water and sodium hydroxide solution but sparingly soluble in organic solvents. However, they are highly soluble in absolute alcohol / dioxin owing to the possession of the –OH (Phenolic) and –COOH (Carboxylic) groups. Schiff base compounds (Scheme 1, 2 and 3) have melting points 258 $^{\circ}$ C, 272 $^{\circ}$ C and 292 $^{\circ}$ C respectively. the magnetic susceptibility value of metal complex compounds with selected ligands were suggested to be paramagnetic copper and Zinc complex compounds with Schiff base Scheme 1 have showed with magnetic moment values 2.31 B.M. and 2.44 B. M. respectively, which are the less than the normal spin values only.

1.1 Synthesis of coordination complexes with selected metal ions at various reaction conditions

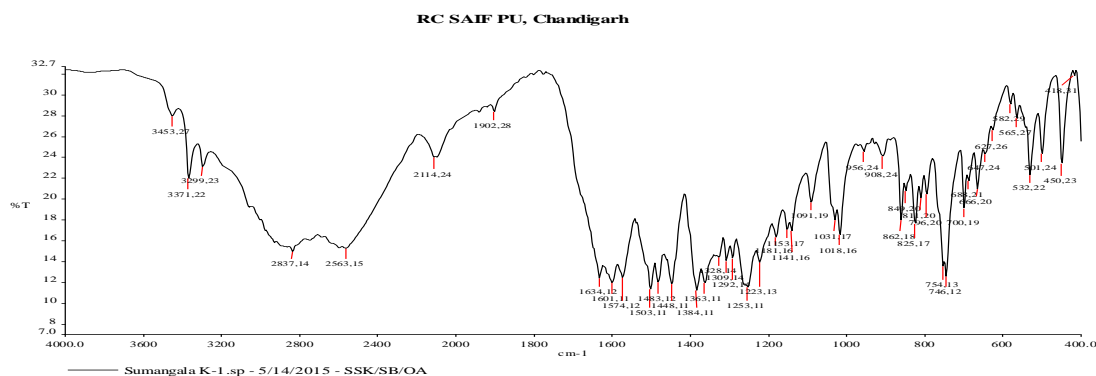
The Schiff base ligands (Scheme 1, 2 and 3) were reacted with the selected metal ions in 2:1 M molar concentrations forming metal complexes of the type $[M(LH)_2]$ where $M = Cu^{II}, Zn^{II}, Co^{II}, Cd^{II}$ and Ni^{II} . Hence, formed metal complexes (Scheme 4, 5 and 6) indicating monomeric nature of metal complexes with OON – donor. All the synthesized metal complexes were sparingly soluble in water and 50% water-ethanol but were fairly soluble in absolute alcohol.

The analytical data of the newly synthesized Schiff bases and their metal complexes were recorded in Table 1. The molecular measurements of the monomeric nature of the complex compounds (Scheme 4, 5 and 6) as shown in Table 2. All the synthesized complex compounds found to be stable up to certain temperature.

1.1 Characterization of the Schiff bases and their metal complexes

FTIR Spectra

The IR spectra of Schiff base ligands (Scheme 1, 2 and 3) and metal complexes (Scheme 4, 5 and 6) were recorded on Perkin – Elmer Spectrum 100 FTIR Spectrometer in KBr pellets in the range 400 – 4000 cm^{-1} . In the Schiff bases spectra, absence of bands due to NH_2 group clearly indicate the formation of Schiff base. In those Schiff bases the IR spectra of ligands showed a characteristic band due to $\nu(N-H)$ at 3250 cm^{-1} . However, a broad band with its center of gravity $\nu(C=N)$ at about 1675 cm^{-1} is observed. The IR spectra of the 3-Aldehydosalicylic acid ligand in its Schiff base compounds exhibit intra-molecular H – bonded carboxylic $\nu(COOH)$ and phenolic $\nu(OH)$ groups stretches at 2910 cm^{-1} and 2710 cm^{-1} , $\nu(C=O)$ carboxylic stretches at 1575 cm^{-1} , $\nu(-OH)$ phenolic stretches at 1575 cm^{-1} . A sharp and strong band in the region of 1617 – 1601 cm^{-1} for $\nu(N=CH)^{[24]}$ in case of ligand is shifted to higher region 1628 cm^{-1} to 1612 cm^{-1} in the spectra of metal complexes 25 indicating coordination through the ligands Nitrogen atom to the metal ion. The formation of a metal Nitrogen band at 578 cm^{-1} for $\nu(M-N)$ 26 indicating the coordination of ligand to the central metal atom through the Nitrogen atom of the ligands. The FTIR-spectroscopic data of the ligands and their metal complexes are given in Table 3.



¹HNMR Spectra

¹HNMR Spectra of ligands and metal complexes were recorded at ambient temperature using Bruker Avance 300 spectrophotometer (300 MHz for ¹HNMR. The chemical shifts are reported in δ , ppm in DMSO – d₆ using tetra methyl silance (TMS) as internal standards. ¹HNMR – Spectra of o-, m- and p- Anisidine ligands the signals of NH₂ protons appear at δ 9.5 ppm to δ 9.2 ppm. these signals shifted to high field in the spectra of the metal complexes and appear at δ 9.5 ppm to δ 9.7 ppm for Organometallic complexes with ligand molecules this indicates the bonding through the Nitrogen atom to the Schiff bases ligands to the central metal ion. The aromatic protons gave ligands at δ 1.2 ppm - δ 1.3 ppm. The ¹HNMR spectroscopic data of the ligands and their metal complexes are given in Table 4.

SSK/SB/OA

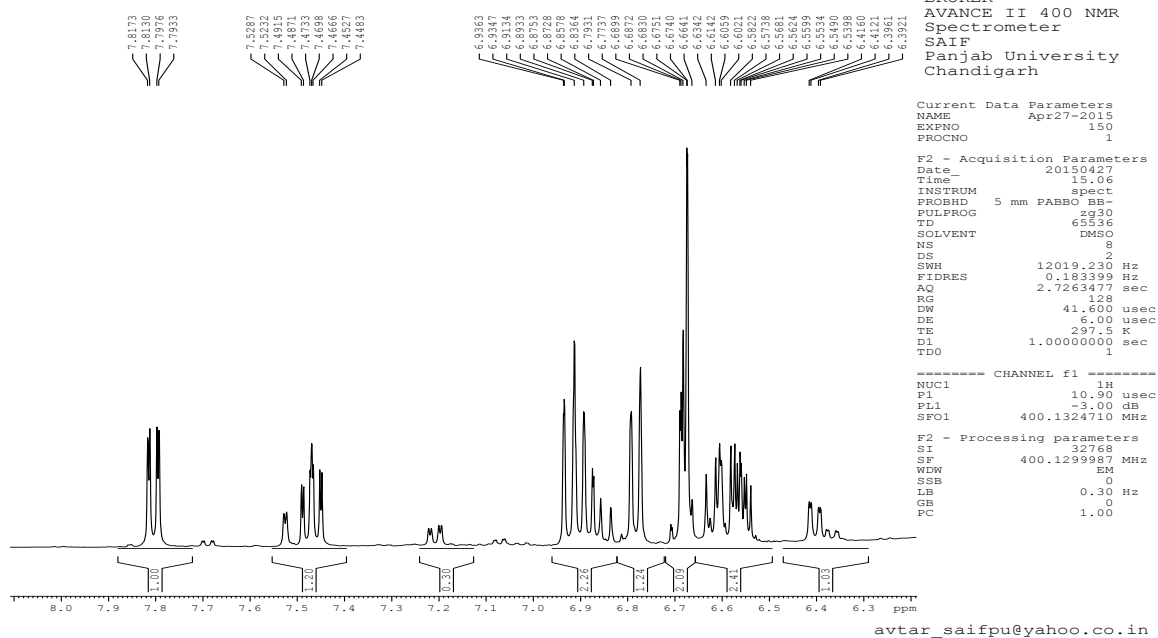


Table 1. The physical and analytical data of ligands and their metal complexes.

Scheme	Molecular Formula	Mol.Wt.	Metal ions	Carbon (Obs)	Hydrogen (Obs)	Oxygen (Obs)	Nitrogen (Obs)
1.	C ₁₅ H ₁₃ O ₄ N	271	---	66.40	4.80	23.6	5.17
2.	C ₁₅ H ₁₃ O ₄ N	271	---	66.40	4.80	23.6	5.17
3.	C ₁₅ H ₁₃ O ₄ N	271	---	66.40	4.80	23.6	5.17
4.	CuC ₃₀ H ₂₂ O ₈ N ₂	601.6	10.57	59.80	3.66	21.28	4.65
	ZnC ₃₀ H ₂₂ O ₈ N ₂	603.4	10.84	59.70	3.65	21.21	4.64
	NiC ₃₀ H ₂₂ O ₈ N ₂	596.7	09.84	60.33	3.69	21.45	4.69
	CoC ₃₀ H ₂₂ O ₈ N ₂	596.9	09.87	60.31	3.69	21.44	4.69
	CdC ₃₀ H ₂₂ O ₈ N ₂	650.2	17.29	55.37	3.38	19.69	4.31
5.	CuC ₃₀ H ₂₂ O ₈ N ₂	601.6	10.57	59.80	3.66	21.28	4.65
	ZnC ₃₀ H ₂₂ O ₈ N ₂	603.4	10.84	59.70	3.65	21.21	4.64
	NiC ₃₀ H ₂₂ O ₈ N ₂	596.7	09.84	60.33	3.69	21.45	4.69
	CoC ₃₀ H ₂₂ O ₈ N ₂	596.9	09.87	60.31	3.69	21.44	4.69
	CdC ₃₀ H ₂₂ O ₈ N ₂	650.2	17.29	55.37	3.38	19.69	4.31
6.	CuC ₃₀ H ₂₂ O ₈ N ₂	601.6	10.57	59.80	3.66	21.28	4.65
	ZnC ₃₀ H ₂₂ O ₈ N ₂	603.4	10.84	59.70	3.65	21.21	4.64
	NiC ₃₀ H ₂₂ O ₈ N ₂	596.7	09.84	60.33	3.69	21.45	4.69
	CoC ₃₀ H ₂₂ O ₈ N ₂	596.9	09.87	60.31	3.69	21.44	4.69
	CdC ₃₀ H ₂₂ O ₈ N ₂	650.2	17.29	55.37	3.38	19.69	4.31

Table 2. The physical constants of synthesized Organometallic complexes and the nature of coordination.

Scheme	Metal complexes	Nature of complexes	Stable up to Temp. in °C.	Donor - Atoms	Donor - Atoms
1	---	---	258°C	---	---
2	---	---	272°C	---	---
3	---	---	292°C	---	---
4	[M(LH) ₂]	Monomeric	232°C & 228°C	OO – donor Monomeric, Dibasic bidentate.	OON-Donor Monomeric, Dibasic tridentate.
5	[M(LH) ₂]	Monomeric	235°C & 232°C	OO – donor Monomeric, Dibasic bidentate	OON-Donor Monomeric, Dibasic tridentate.
6	[M(LH) ₂]	Monomeric	230°C & 220°C	OO – donor Monomeric, Dibasic bidentate	OON-Donor Monomeric, Dibasic tridentate.

Table 3. IR- Spectroscopic data (cm-1) of the ligands and its Cu(II) & Zn(II) complexes.

Scheme	Functional group	IR- Values in cm-1	Scheme	Functional group	IR- Values in cm-1
Scheme 1	√(-COOH)	2910 cm ⁻¹	Scheme 4	√(-COO-)	1748 cm ⁻¹
	√(-OH)	2710 cm ⁻¹		√(C=N)	1628 cm ⁻¹
	√(C=N)	1628 cm ⁻¹		√(C-H)	3000 cm ⁻¹
	√(C-H)	3000 cm ⁻¹		√(C=O)	1695 cm ⁻¹
	√(C=O)	1695 cm ⁻¹		√(M-N)	578 cm ⁻¹
			√(M-O)	440 cm ⁻¹	
Scheme 2	√(-COOH)	2910 cm ⁻¹	Scheme 5	√(-COO-)	1748 cm ⁻¹

	$\sqrt{(-OH)}$	2710 cm^{-1}		$\sqrt{(C=N)}$	1628 cm^{-1}
	$\sqrt{(C=N)}$	1628 cm^{-1}		$\sqrt{(C-H)}$	3000 cm^{-1}
	$\sqrt{(C-H)}$	3000 cm^{-1}		$\sqrt{(C=O)}$	1695 cm^{-1}
	$\sqrt{(C=O)}$	1695 cm^{-1}		$\sqrt{(M-O)}$	440 cm^{-1}
				$\sqrt{(M-N)}$	578 cm^{-1}
Scheme 3	$\sqrt{(-COOH)}$	2910 cm^{-1}	Scheme 6	$\sqrt{(-COO-)}$	1748 cm^{-1}
	$\sqrt{(-OH)}$	2710 cm^{-1}		$\sqrt{(C=N)}$	1628 cm^{-1}
	$\sqrt{(C=N)}$	1628 cm^{-1}		$\sqrt{(C-H)}$	3000 cm^{-1}
	$\sqrt{(C-H)}$	3000 cm^{-1}		$\sqrt{(C=O)}$	1695 cm^{-1}
	$\sqrt{(C=O)}$	1695 cm^{-1}		$\sqrt{(M-N)}$	578 cm^{-1}
				$\sqrt{(M-O)}$	440 cm^{-1}

Table 4. ¹HNMR Chemical Shifts of the ligands and its Cu (II) complexes.

Compound	Aromatic H	-CH=N	-OCH ₃	-NH ₂
Scheme 1	7.1 – 8.0 (m)	δ 10.3 (s)	---	δ 7.6 - δ 7.8
Scheme 2	7.1 – 8.0 (m)	δ 10.3 (s)	---	δ 7.6 - δ 7.8
Scheme 3	7.1 – 8.0 (m)	δ 10.3 (s)	---	δ 7.6 - δ 7.8
Scheme 4	7.1 – 8.0 (m)	δ 10.3 (s)	δ 13.7 (s)	---
Scheme 5	7.1 – 8.0 (m)	δ 9.7 (s)	δ 13.7 (s)	---
Scheme 6	6.9 – 8.0 (m)	δ 9.5 (s)	δ 13.2 (s)	---

Table 5. Antibacterial screening data of Schiff base and their metal complexes Standard = Gentamycin: Diameter of inhibition zone (mm): Concentration in (ppm).

No.	Scheme	E-Coil			S.aureus			S.Fecalis		
		25	50	100	25	50	100	25	50	100
1	Scheme 1	13	14	18	-	12	14	-	-	-
2	Scheme 2	13	14	18	12	13	15	14	14	17
3	Scheme 3	13	14	18	12	13	15	14	14	17
4	Scheme 4 with Cu(II)	28	32	35	14	12	16	16	15	16
5	Scheme 4 with Zn(II)	14	13	16	11	12	14	12	13	14
6	Scheme 5 with Cu(II)	24	28	31	15	14	16	15	14	16
7	Scheme 5 with Zn(II)	15	14	16	11	14	13	11	12	13
8	Scheme 6 with Cu(II)	28	32	35	14	12	16	16	15	16
9	Scheme 6 with Zn(II)	14	13	16	11	12	14	12	13	14
10	Standard	20	23	20	12	12	14	18	20	19
11	DMSO(-) = Not	-	-	-	-	-	-	-	-	-

Table 6. Antifungal screening data of Schiff base and their metal complexes Standard = Nystaline: Diameter of inhibition zone (mm): Concentration in (ppm).

No.	Scheme	A.Niger			T. Polysponum		
		25	50	100	25	50	100
1	Scheme 1	12	12	15	12	15	19
2	Scheme 2	13	13	16	11	15	17
3	Scheme 3	13	13	16	12	15	19
4	Scheme 4 with Cu(II)	-	-	-	12	15	16
5	Scheme 4with Zn(II)	-	-	-	11	13	18

6	Scheme 5 with Cu(II)	-	-	-	12	14	16
7	Scheme 5 with Zn(II)	-	-	-	11	12	14
8	Scheme 6 with Cu(II)	-	-	-	11	13	18
9	Scheme 6 with Zn(II)	-	-	-	12	14	16
10	Standard	-	-	-	-	-	-
11	DMSO (-) = Not Measurable	-	-	-	-	-	-

CONCLUSIONS

As per the study on the citation of metal- complexes , the three Schiff base ligands of o-, m- and p- Anisidine, derived from 3-Aldehydosalicylic acid (Scheme 1,2 and 3) and their metal complexes (Scheme 3,4 and 6) with Cu (II), Ni (II), Co (II), Cd (II) and Zn (II) have been synthesized in different reaction conditions. The Schiff base ligands act as monobasic bidentate OO- donor ligand forms monometallic complex compounds at lower pH ranges of the type $[M(LH)_2]$ where $M= Cu^{II}, Zn^{II}, Co^{II}, Cd^{II}$ and Ni^{II} and the ligands also act as a dibasic tridentate OON- donor at higher pH range forming Monometallic complex compounds of type $[ML_2]$ with all selected metal ions. In the present investigations, the IR – Spectra of the metal complexes a sharp band appears at 1470 cm^{-1} to 1430 cm^{-1} (Scheme 4, 5 and 6) reveals that the non-involvement of the methyl V(-CH₃) and Methoxyl V(-OCH₃) groups in coordination. Here in these metal complexes the IR report reveals the involvement of carboxylic O- atom, Phenolic O- atom by exhibiting the $V_s(COO)$ and $V_{as}(COO)$ stretches of carboxylate group in the range $V_{1560}\text{ cm}^{-1}$ to $V_{1650}\text{ cm}^{-1}$ (i.e., at $V_{1600}\text{ cm}^{-1}$) and $V_{1340}\text{ cm}^{-1}$ to $V_{1430}\text{ cm}^{-1}$ (i.e., at $V_{1400}\text{ cm}^{-1}$) respectively. the energy difference between $V_{as}(COO)$ and $V_s(COO)$ is more than 200 cm^{-1} indicates the monodentate nature of the carboxyl ate moiety.^[26] The formation of a Metal –Nitrogen (M-N) band is supported by the presence of band at 578 cm^{-1} for V (M-N) indicating the coordination of ligand with central metal atom through the Nitrogen atom of the ligand.

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