

SYNTHESIS AND ANTIMICROBIAL ACTIVITY STUDY OF NOVEL SCHIFF BASE LIGAND (E)-N-(5,6-DIMETHOXPYRIMIDIN-4-YL)-4-((2-HYDROXY-5-NITROBENZYLIDEE) AMINO) BENZENE SULPHONAMIDE AND THEIR TRANSITION METAL COMPLEXES

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Abstract:

The new Schiff base ligand (L1H) (E)-N-(5,6-dimethoxypyrimidin-4-yl)-4-((2-hydroxy-5-nitrobenzylidene)amino) benzene sulphonamide (DMPHNAB) was synthesized from 4-amino-N-(5,6-dimethoxypyrimidin-4-yl) benzene sulphonamide and 2-hydroxy-5-nitrobenzaldehyde and the geometry of Schiff base was characterized and determined by proton nuclear magnetic resonance (¹H-NMR), mass, Fourier transform infrared (FT-IR), and ultraviolet-visible (UV-Vis) spectroscopy. By the reaction of metal ions with as-prepared Schiff base, Schiff base complexes of Ni (II), Co (II), Cu (IV), Zn (II), and Mn(II) were prepared. The results showed that synthesized complexes offered 1:2 metal-ligand ratios. Furthermore, the Schiff complexes of Ni (II), Zn (II), Cu (II), and Mn (II) are octahedral. Moreover, the Schiff base and its metal complexes have been verified in vitro against *S. Aureus*, *E. coli*, *Candida albicans*, and *A. Niger* in order to assess their antibacterial potential. The results suggest that biological activity increases in the reaction of complexation.

Keyword: Schiff Bases, metal complexes, Biocidal Activity, spectral analysis.

1. Introduction:

Schiff bases contain azomethine (-C=N-) bonds and are typically derived from the condensation of primary aliphatic/aromatic/heteroaromatic amines with carbonyl compounds (aldehydes/ketones). Remarkable attention was drawn to the chelating ability of these compounds and their analytical and biological applications. The complexes containing O, N, donor atoms are very important due to their strong antibacterial and anticancer activity. [1].

While several classes of antibacterial compounds are currently active, resistance by microorganisms to these drugs is constantly emerging. To prevent this important medical problem, the development of new types of antibacterial agents or the extension of the bioactivity of previous drugs is a very relevant challenge [2].

The development of new and different antibacterial drugs is therefore a very important goal and a significant amount of research program effort is aimed at designing new agents. [3] Synthesis and characterization of metal complexes with organic bioactive ligands, especially of metal complexes with Schiff bases, is one of the promising fields of research. In present work, we report here the synthesis, characterization, antibacterial activity of Schiff base derived from 4-amino-N-(5, 6-dimethoxypyrimidin-4-yl) benzene sulphonamide and 2-hydroxy-5-nitrobenzaldehyde. The structures of these Schiff bases were confirmed by UV, FT-IR, ¹H-NMR, and Mass spectroscopic tools and additionally by Elemental analysis.

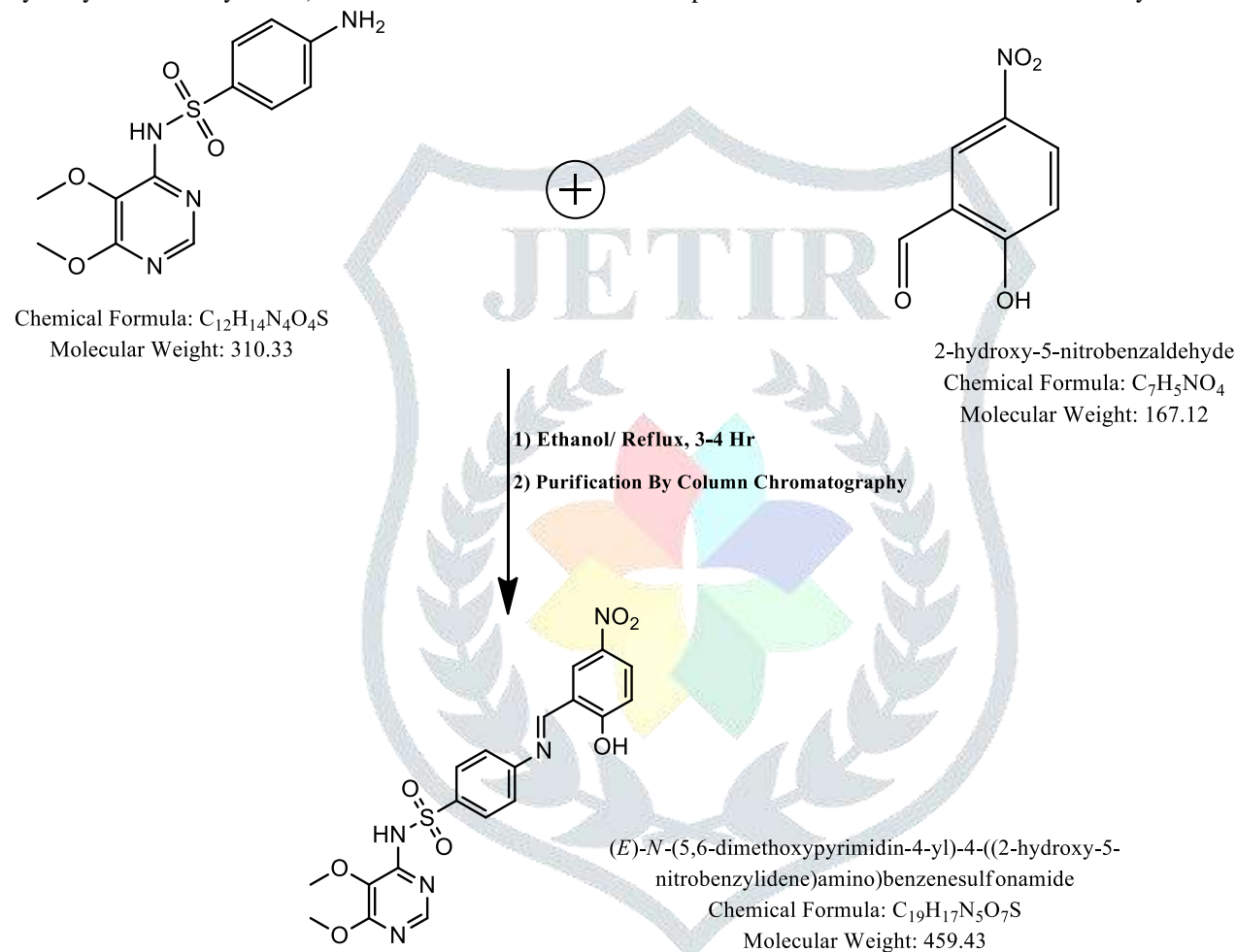
2. EXPERIMENTAL

2.1 Materials and methods:

The chemicals used are 4-amino-N-(5,6-dimethoxypyrimidin-4-yl) benzene sulphonamide (Merck, AR grade), and 2-hydroxy-5-nitrobenzaldehyde (Merck, AR grade), Cobalt(II) chloride dehydrate (Merck, AR grade), Nickel (II) chloride hexahydrate (Sigma Aldrich), Copper(II) chloride dehydrate (Sigma Aldrich), Anhydrous zinc(II) chloride, Manganese(II) chloride tetra hydrate (Merck, AR grade),

Synthesis of ligands and metal complexes:

2-hydroxy-5-nitrobenzaldehyde drop wise was added to a stirred solution of 4-amino-N-(5, 6-dimethoxypyrimidine-4-yl) benzene sulphonamide (1.0 eq) in ethanol (10 ml) at room temperature and then heated to reflux until reaction completion. The reaction progress was controlled by TLC. After completion of the reaction obtained, solids were filtered and dried well, which was further purified in dichloromethane by flash column chromatography to give the product (E)-N-(5, 6-dimethoxypyrimidine-4-yl)-4-(2-hydroxy-5-nitrobenzylidene)amino benzene sulphonamide as a yellow solid.



Scheme 1: Synthesis of schiff base ligand (E)-N-(5,6-dimethoxypyrimidin-4-yl)-4-(2-hydroxy-5-nitrobenzylidene)amino)benzenesulfonamide

In ethanol solutions (10 mL) of ligand L_1H ethanol solutions (10 mL) of metal salts were added with constant stirring in a 1:2 ratio. The mixture was stirred and filtered for 2 h. By filtration, the precipitates have been isolated. The precipitates were purified by recrystallization in methanol; a coloured solid crystal was isolated, filtered and dried out.

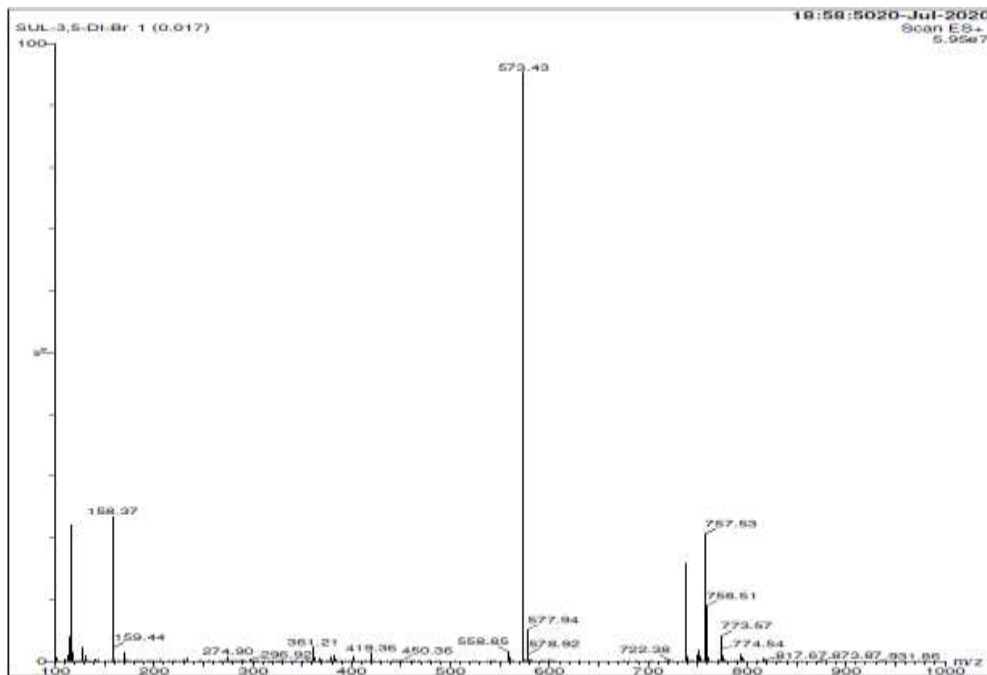


Figure 1: Mass spectra of Schiff base ligand

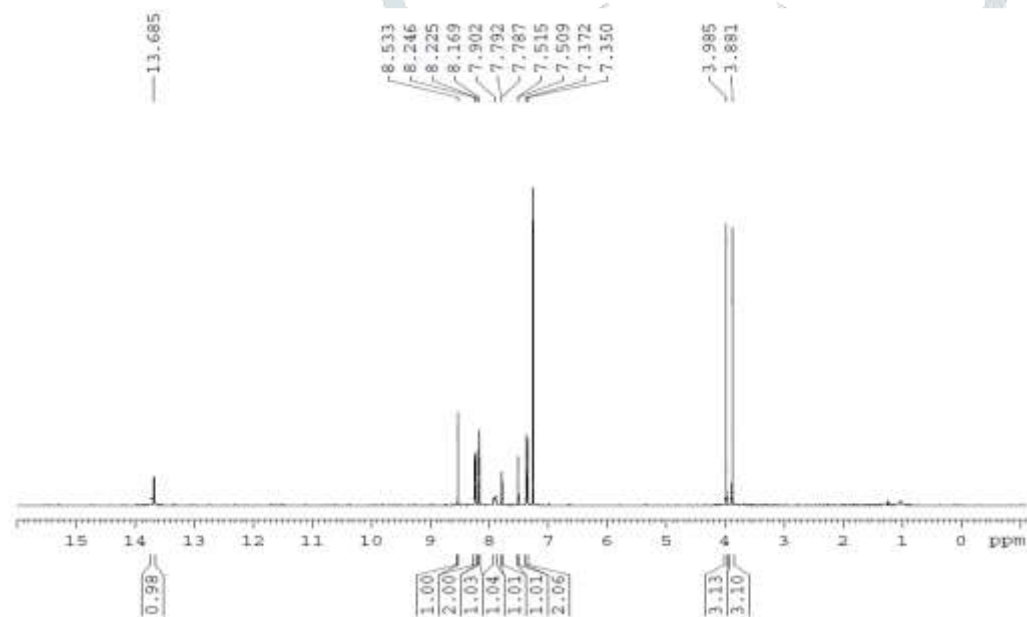


Figure 2: NMR spectra of Schiff base ligand

3. Results and Discussion:

3.1 Physical measurements

NMR spectral measurements were performed in Bruker AMX 400-MHz. Elemental microanalysis (C, H, and N, S, O) were carried out on Thermo finning, Italy (Flash EA 1112 series). Conductivity measurements using a Jenway 4071 digital conductivity were performed with DMSO solutions. In JEOL, Japan JES-FA200 spectrometry, ESR spectra of Cu complexes were performed at LT solution form with X-band UV-visible spectra of compounds were carried out on Agilent technologies carry 100UV-vis spectrometer.

3.2 Physical characteristics and elemental analysis

The elemental analysis shown in Table-1 shows that, with respect to L_1H and metal salts $MX_2 \cdot xH_2O$ {where $M=Co(II), Ni(II), Cu(II)$ and $Zn(II)$ }, all the metal complexes have 2:1 stoichiometry with respect to ligands and metal salts respectively. and are dark coloured amorphous substances soluble in DMF and DMSO.

Details on physical, analytical, magnetic susceptibility and molar conductance of the ligands and their complexes of mixed ligands.

Table 1; Physical characteristics and Elemental analysis data:

Compounds	Molecular weight	Colour	M.P (°C)	% Found (Calc.)						% Yield	μ_{eff} (B.M)
				C	H	N	S	O	M		
(DMPHNAB) L_1H	459.53	yellow	116	60.75	5.06	8.86	-----	25.31	-----		----
$[Mn(L_1)_2(H_2O)_2]$	1007.73	Blackish green	205	46.05	3.95	5.03	19.16	19.19	6.58	82	5.36
$[Co(L_1)_2(H_2O)_2]$	1011.33	Buff	250	45.83	3.93	5.01	19.07	19.09	7.03	67	3.59
$[Ni(L_1)_2(H_2O)_2]$	1011.49	green	210	45.85	3.94	5.01	19.08	19.10	7.00	78	2.89
$[Cu(L_1)_2(H_2O)_2]$	1016.34	Brown	214	45.58	3.91	4.98	18.97	18.99	6.9	64	1.56
$[Zn(L_1)_2(H_2O)_2]$	1018.1	Bright yellow	216	45.48	3.90	4.97	18.92	18.95	7.74	72	0.00

3.3 Infrared spectra and NMR Spectra

At 1610 cm^{-1} in the Schiff base $\nu(C=N)$ stretching band is observed. This band shifts by 10 to 30 cm^{-1} to lower energy in chelates, showing azomethine nitrogen coordination. The frequencies assigned to $\nu(C-N)$ stretching in the range are 1145-1165 cm^{-1} [4-5]. Conclusive evidence of bonding is also shown by the observation that new bands are assigned to $\nu(M-O)$ and $\nu(M-N)$ stretching vibrations at 455-460 cm^{-1} and 514-525 cm^{-1} in the metal complex spectra respectively and are not observed in the ligand spectra [7-10]. The presence of a sharp band corresponding to the remaining hydroxyl group at 3400 cm^{-1} is hidden by the presence of water molecule bands. For the most complexes and a very wide band which was associated with coordinated or solvent water molecules, this was seen at about 3400-3500 cm^{-1} area. The formation of ligand was confirmed by the presence of peak at 8.5 due to $CH=N$ and a peak at 4.1 due to Phenolic $-OH$ group. The ligands IR spectra gives the strong band at 1610.09 and 3076.53 which are attributed to stretching frequency of $C=N$ of azomethine and $-OH$ groups respectively as shown in table-2.

The Ni-complex of Schiff base shows a lower shift of 30-40 cm^{-1} for $C=N$ due to co-ordination through azomethine N also a new bands are observed for M-N and M-O.

Sr. No.	Compound	$\nu(OH)$ cm^{-1}	$\nu(OH)$ Water cm^{-1}	$\nu(C=N)$ cm^{-1}	$\nu(M-O)$ cm^{-1}	$\nu(M-N)$ cm^{-1}
1	(DMPHNAB) SB1(L_1H)	3076.53	-----	1610.09	-----	-----
2.	$[Ni(L^1)_2(H_2O)_2]$	-----	3699	1523.95	551	482
3.	$[Co(L^1)_2(H_2O)_2]$	-----	3610.49	1556.38	659.61	516.89
4.	$[Cu(L^1)_2(H_2O)_2]$	-----	3448.49	1569.95	636.47	574.75
5.	$[Zn(L^1)_2(H_2O)_2]$	-----	3537.84	1600.81	644.18	520.74
6.	$[Mn(L^1)_2(H_2O)_2]$	-----	3446.17	1539.88	496.58	454.15

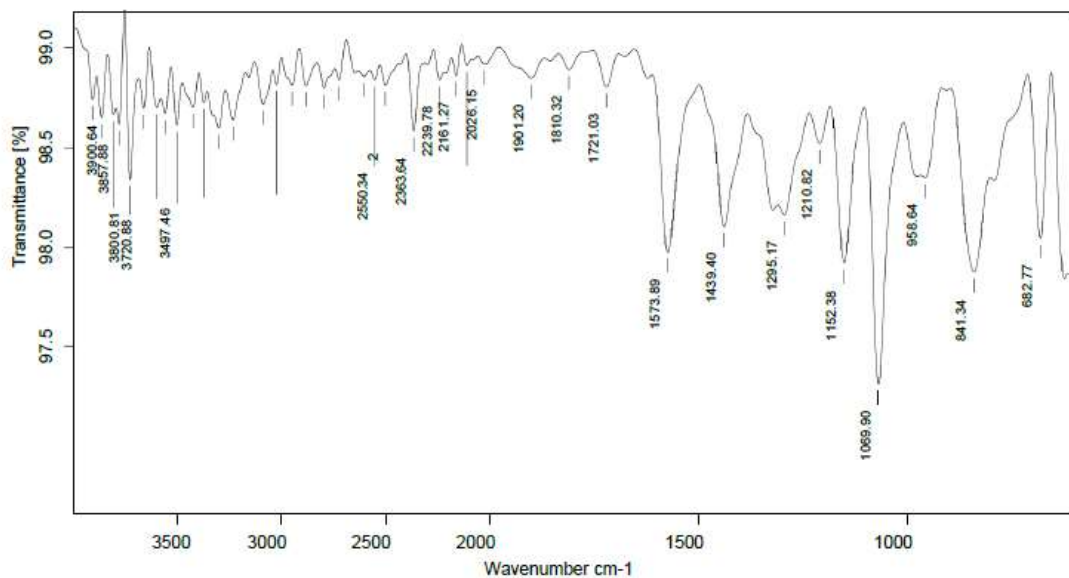


Fig 3: IR spectra of sulpho-5-nitro Schiff base

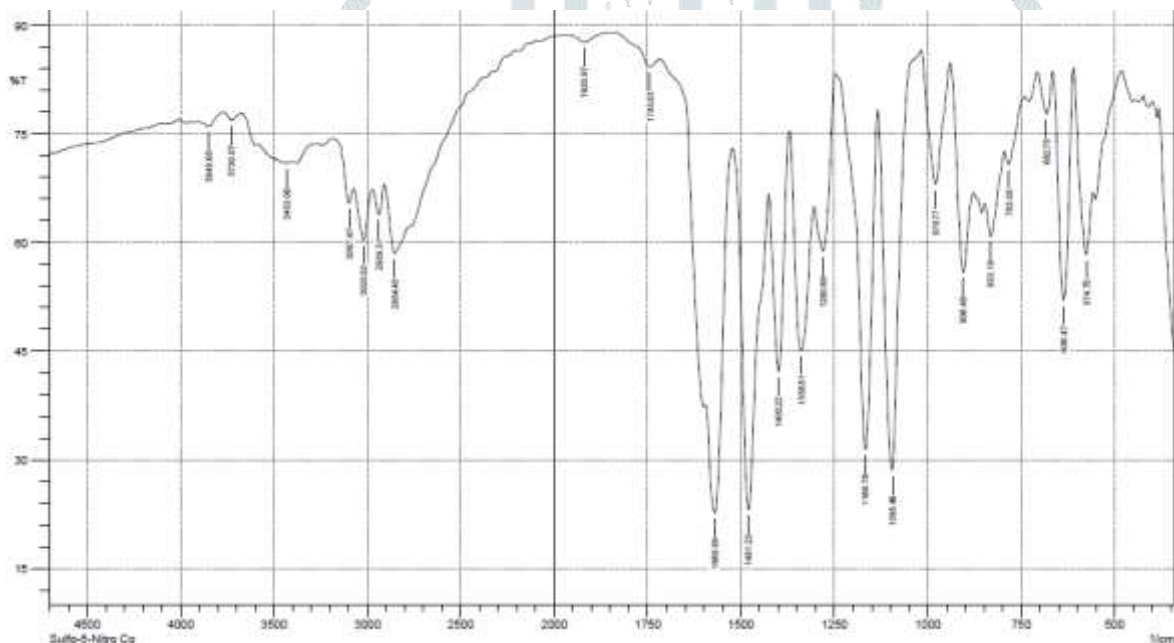


Fig 4: IR spectra of sulpho-5-nitro -Co Complex

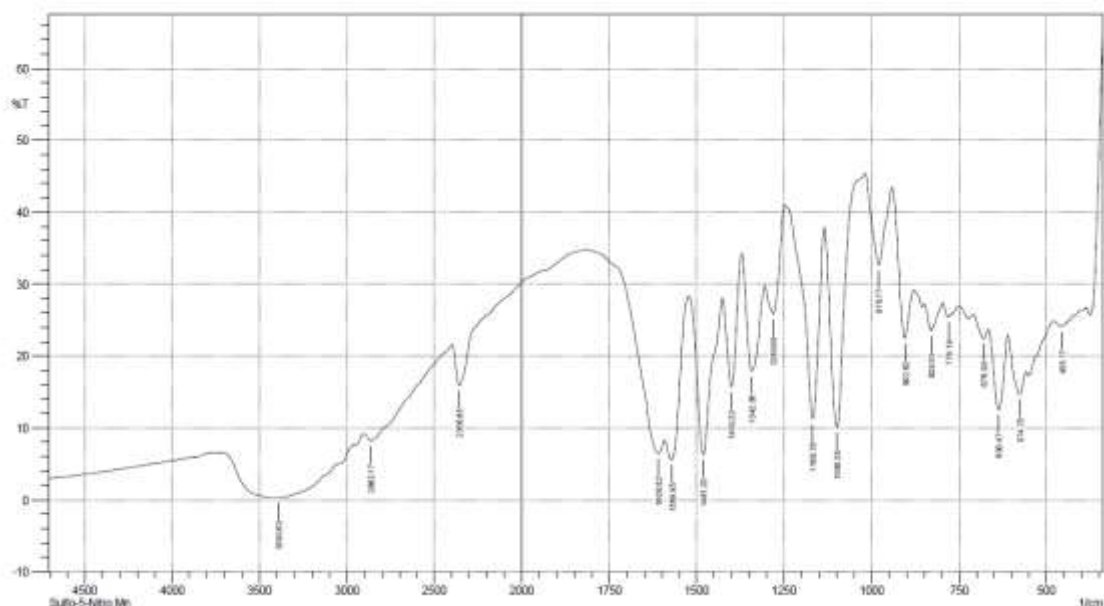


Fig 5: IR spectra of sulfo-5-nitro -Mn Complex

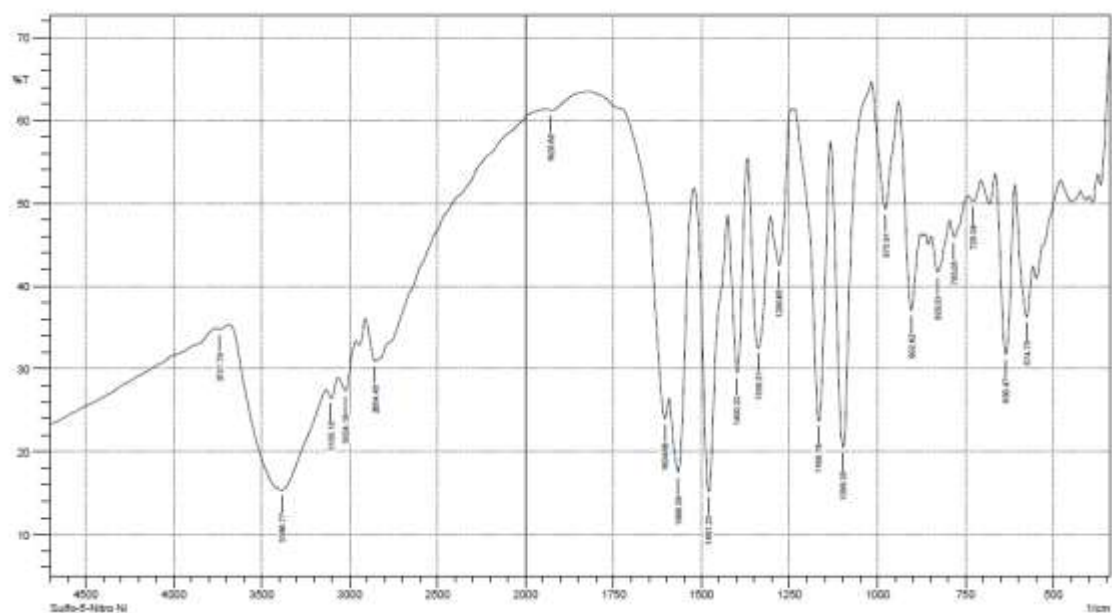


Fig 6: IR spectra of sulfo-5-nitro -Ni Complex

3.4 Magnetic Measurements:

The values of the magnetic moment are useful in the assessment of results given by other structural analysis techniques. The Mn (II) complex shows 5.88-5.92 B.M. magnetic moment, Mn (II) complex shows 5.88-5.92 B.M. magnetic moment, five unpaired electrons that suggest octahedral geometry at room temperature [11]. Zn (II) Complex shows a diamagnetic nature and is characterized by octahedral geometry.

3.5 UV-Visible study

UV-Visible spectra of all the synthesized ligands and their metal complexes were recorded in Solvent DMSO. Due to the presence of C=N group in the compounds band at 373-384 nm for L₁H was observed and it corresponds to $\pi-\pi^*$ transition [12,13]. Because of the keto-amine transformation of these compounds, the wide absorption band was observed in the 490-495 nm range. The absorption of the higher energy region confirms the compound's keto-imine form, whereas the absorption of the lower energy region shows the enol-imine form. For compounds having azomethine groups in which the hydroxyl group is present at ortho position t, this behaviour was expected.

Two bands were observed at 249.1 nm (40144.52 cm⁻¹) and 401.9 nm (24881.81 cm⁻¹) in the Co(II) complex. With regard to the spectrum of the Schiff base ligand, this was a shift towards a longer wavelength. The band was due to intra ligand transition at 249.1 nm, and the band was due to d-d transition at 401.9 nm for ${}^3T_{1g}(F) \rightarrow {}^3T_{2g}$, which is within the range for octahedral configuration range as reported in many octahedral cobalt(II) complexes.

3.6 Molar conductivity

Molar conductivities of all metal complexes were taken in DMSO due to partial solubility in common organic solvents, to find out electrolytic nature of the complexes. The conductance in DMSO of metal complexes was within the range of 69-79 mhos cm² mol⁻¹, as shown in Table 1. This shows the non-electrolyte behaviour of all. It is therefore suggested that the complex formed is in the 2:1 (ligand: metal) ratio as seen in fig..

Complex	Conductance (mhos)	Specific conductance(mhos cm ⁻¹)	Molar conductance (mhos cm ² mol ⁻¹)
[Cu(L ¹) ₂ (H ₂ O) ₂]	0.04	3.12×10^{-3}	31.20
[Ni(L ¹) ₂ (H ₂ O) ₂]	0.12	9.3×10^{-3}	93.60
[Zn(L ¹) ₂ (H ₂ O) ₂]	0.09	7.02×10^{-3}	70.20
[Co(L ¹) ₂ (H ₂ O) ₂]	0.07	5.4×10^{-3}	54.60
[Mn(L ¹) ₂ (H ₂ O) ₂]	0.03	2.34×10^{-3}	23.40

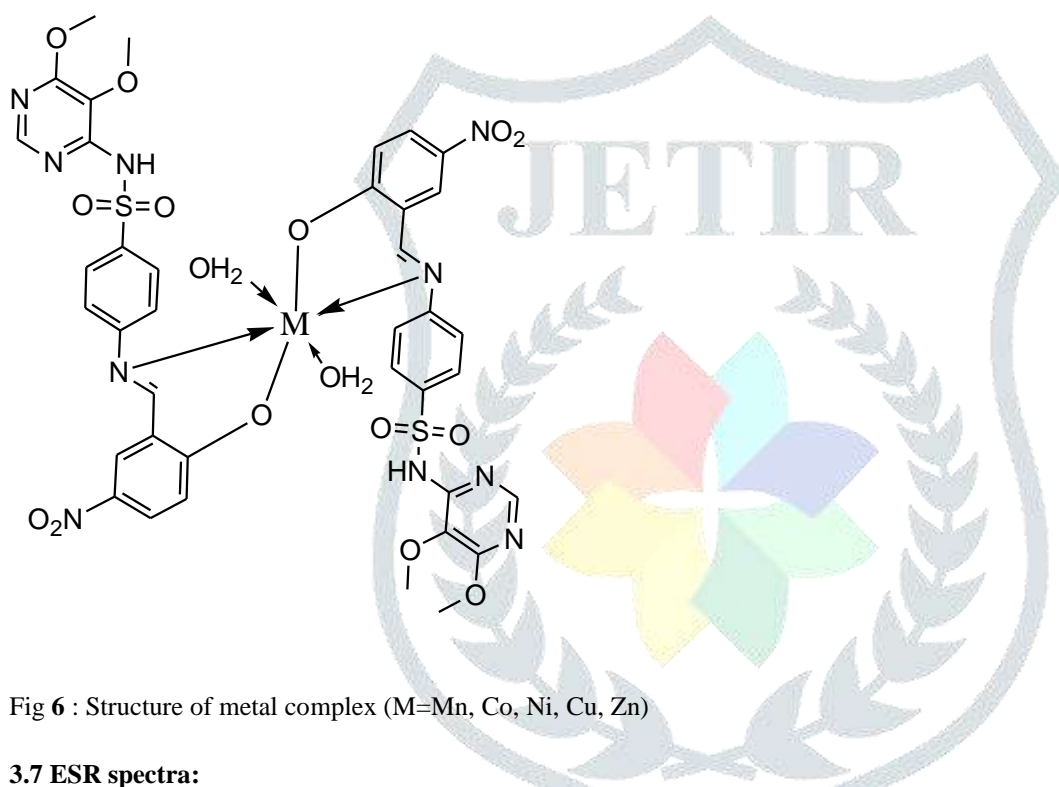


Fig 6 : Structure of metal complex (M=Mn, Co, Ni, Cu, Zn)

3.7 ESR spectra:

As shown in the figure, the X-band ESR spectra of [Cu (L₁)₂(H₂O)₂] were recorded at room temperature (300 K) in solid state. The spectrum in the higher magnetic field exhibits an intense absorption band. Due to the molecule's sliding motion, the nature of the spectrum is isotropic. [14] The magnetic anisotropy of ESR is explained using the g component. The value of g_{avg} is determined using the formula

$$g_{avg} = 1/3(g^{||} + 2g^{\perp})$$

Table 4: ESR spectral data of complex

Complex	g^{\perp}	$g^{ }$	g_{avg}	G
[Cu(L ¹) ₂ (H ₂ O) ₂]	2.034	2.134	2.067	4.151

The spectrum displays asymmetric bands with two g values. The $g^{||} > g^{\perp} > 2.00277$ pattern suggests that the unpaired electron is primarily present in the orbital dx²-y², and due to low symmetry, there is a chance of dz² orbital mixing.

3.8 Antibacterial activity:

The antibacterial activity was measured by agar cup method[15]. The synthesized metal complexes and ligands are screened against gram positive and gram negative bacteria viz. Escherichia Coli and Staphylococcus aureus. The activity is compared with standard penicillin and negative control DMSO .The order of activity can be summarized as follows.

Table 7 : Antimicrobial activity data of the ligands L¹H and their complexes.

Schiff base/complex	Zone of Inhibition(mm)			
	C. albicans	A. Niger	E. coli	S. Aureus
(DMPHNAB) L ₁ H	42	42	42	42
[Ni(L ¹) ₂ (H ₂ O) ₂]	23	42	34	20
[Co(L ¹) ₂ (H ₂ O) ₂]	44	44	30	24
[Cu(L ¹) ₂ (H ₂ O) ₂]	42	40	32	22
[Zn(L ¹) ₂ (H ₂ O) ₂]	44	42	10	-----
[Mn(L ¹) ₂ (H ₂ O) ₂]	44	39	32	20
clotrimazole	20	22	-----	-----



Fig.7 : Zone of inhibition of metal complexes

4. Conclusion:

In this work, the metal chelate complexes have been prepared from 4-amino(5,6-dimethoxypyrimidine-4-yl) benzene sulphonamide and 2-hydroxy-5-nitro benzaldehyde. The characterisation of compounds are described by Mass spectra-Vis spectra, FT-IR and H¹ NMR spectroscopic techniques. Exploration of the results of antimicrobial activities are in the order, Complexes>ligand>standard. The results revealed octahedral geometries for the Ni(II),Zn(II),Cu(II),Mn(II) and Co(II) complexes.

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