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TETRADENTATE SCHIFF BASE
LIGAND

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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL INVESTIGATION OF Ni[II], Cu[II] Co[II], Zn[II], Mn[II] METAL COMPLEXES OF TETRADENTATE SCHIFF BASE LIGAND

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ABSTRACT: Biological active Schiff base (HPMBP) was prepared from 2,4-Diamino-6-hydroxypyrimidine and 5-bromo-2-hydroxybenzaldehyde by condensation method. A series of novel Ni[II], Cu[II] Co(II), Zn(II) and Mn(II) complexes have been synthesized from Schiff base ligand (HPMBP). The structural features and physical properties of Schiff base ligand (HPMBP) and their metal complexes were explored from spectral characterization techniques such as ¹H NMR, ¹³C NMR, Mass, FT-IR spectra, P-XRD and TGA. The spectral analysis data shows that the metal complexes have composition of ML(1:1) type. The P-XRD data propose monoclinic crystal system for Ni(II), Co(II), Zn(II), Mn(II) complexes and orthorombic crystal system for Cu(II) complex. The bio-efficiency of ligand and its transition metal complexes have been tested against three gram +ve /gram -ve bacteria (*Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*) and four fungi (*Penicillium chrysogenum*, *Trichoderma viride*, *Aspergillus niger* and *Candida albicans*) in vitro to examine their microbial activity. The bioactivity data reveals that the metal complexes showed good antifungal and antibacterial activity than the Schiff base ligand (HPMBP).

KEYWORDS: 2,4-Diamino-6-hydroxypyrimidine, Schiff base, Metal complexes. Bio-efficiency

INTRODUCTION:

Schiff bases are organic compounds having azometine (-CH=N-) group which is derived from aromatic amine and aromatic aldehyde or ketone by elimination of water molecule [1]. The coordination chemistry of Schiff base ligand and its transition metal complexes has come to be interesting area for researcher due to their significant impact on

environment as well as human life [2]. Schiff bases ligands are identified as acceptable antibacterial agents [3]. The tetradentate Schiff base ligands with O, N donor atoms are an interesting class of compound because of their wide range of use in synthesis of biochemical, agrochemicals and medicine [4]. On the other hand transition metal complexes have remarkable range of applications such as antimicrobial, antitubercular, antioxidant, antimalarial activity, antiviral, anticancer, antifungal, antianalgesic, anti-inflammatory, sedative, antipyretic, antiproliferative, use in organic battery, photostabilizer, electrode, photodetector, opto-electronic, solar filter, electrochromic device is due to the presence of the (HC=N) azomethine group [5-12]. The Schiff base ligands and their transition metal complexes are very acceptable as catalysts in various biological systems. The pyrimidine ring containing Schiff base have a exclusive medicinal applications [13]. The bioefficiency of these Schiff base molecules in biological aspects encouraging the research scholars to synthesis of new Schiff base compound and to examine the bio-activity in vivo and in vitro analysis [14].

In view of miscellaneous function of Schiff base ligand and their metal complexes, the metal complexes of Ni(II), Cu(II), Co(II), Zn(II) and Mn(II) with Schiff base ligand derived from 2,4-Diamino-6-hydroxypyrimidine and 5-bromo-2-hydroxybenzaldehyde have been synthesized and investigated by ^1H NMR, ^{13}C NMR, Mass, FT-IR spectra, P-XRD and TGA. The Schiff base ligand and its metal complexes have been screened for their antibacterial and antifungal activities by using the agar disk diffusion method against preferred bacteria and fungi.

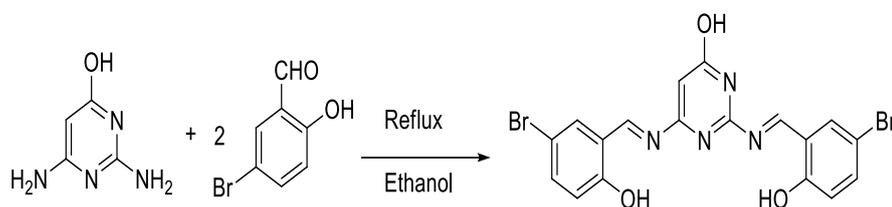
EXPERIMENTAL:

All chemicals used for the synthesis of Schiff base ligand and its complexes were pure and AR grade. FT-IR spectra was recorded on Bruker AlphaT FT-IR spectrophotometer using KBr disc. ^1H and ^{13}C NMR spectra was recorded on Bruker 500MHz NMR instrument in CDCl_3 . A mass spectrum was recorded on Bruker Esquire 3000 mass spectrometry. The thermo gravimetric analysis was performed on Perkin Elmer TA/SDT-2960 and P-XRD were recorded on Philips 3701.

Preparation of Schiff base:

2,2'-(1E,1'E)-(6-hydroxypyrimidine-2,4-diyl)bis(azan-1-yl-1-ylidene)bis(methan-1-yl-1-ylidene) bis(4-bromo phenol) (HPMBP) was prepared by gradually mixing hot alcoholic solution (20ml) of 2,4-Diamino-6-hydroxypyrimidine (0.005 mol) with hot alcoholic solution (20ml) of 5-bromo-2-hydroxybenzaldehyde (0.01 mol) along with adding 2-3 drops

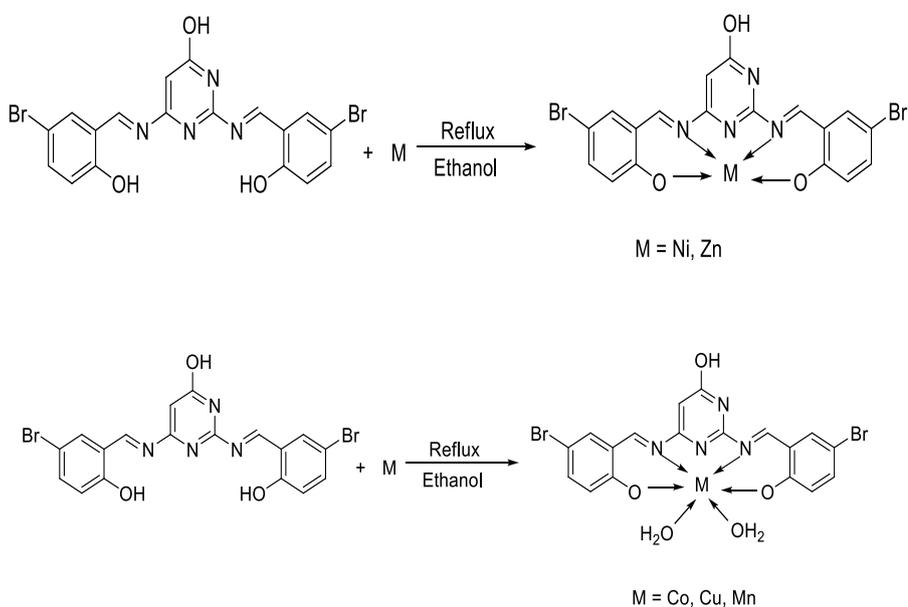
of HCl with constant stirring. The above reaction mixture was refluxed at 80-85°C for about 4 hrs. On cooling, the solid yellow color product was formed, which was filtered and washed thoroughly with cold ethanol and dried under vacuum. (Yield =71 %.)



Scheme 1. Synthesis of Schiff base ligand (HPMBP)

Preparation of metal complexes:

The ethanolic solution (25 ml) of the Schiff base ligand (0.001 mol) and ethanolic solution (25 ml) of the corresponding metal acetate salt (0.001 mol) was mixed together with stirring. The pH of reaction mixture was maintained in between 7-8 by adding few drops of 10% alcoholic solution of ammonia. The reaction mixture was refluxed about 3-4 hrs at 80-90 °C. On cooling, solid colored products obtained. The ppt. was filtered, washed with ethanol and dried under vacuum. (Yield 51-65%.)



Scheme 2. Synthesis of Ni[II], Cu[II], Co(II), Zn(II) and Mn(II) complexes

RESULTS AND DISCUSSION:

All metal complexes having different colours, insoluble in ethanol and methanol.

Table 1: Physical and analytical data of ligand (HPMBP) and its metal complexes

Sr. No	Ligand/Metal Complexes	Colour	Yield (%)	Elemental Analysis Found % [Calc. %]				
				C	H	N	Br	M
1	HPMBP	Yellow	71	43.84 [43.93]	2.38 [2.46]	11.33 [11.38]	32.39 [32.47]	-- --
2	[Ni(II) L]	Wine	65	39.39 [39.36]	1.84 [1.82]	1.21 [10.20]	29.12 [29.16]	10.69 [10.69]
3	[Cu(II) L(H ₂ O) ₂]	Green	64	36.66 [36.60]	2.39 [2.37]	9.50 [9.49]	27.10 [27.09]	10.78 [10.75]
4	[Co (II) L(H ₂ O) ₂]	Brown	60	36.95 [36.90]	2.41 [2.40]	9.58 [9.55]	27.31 [27.30]	10.07 [10.6]
5	[Zn(L)]. 2H ₂ O	Mustard	53	38.92 [38.90]	1.81 [1.80]	10.09 [10.8]	28.77 [28.75]	11.77 [10.75]
6	[Mn (II) L(H ₂ O) ₂]	Yellow	51	37.21 [37.20]	2.43 [2.41]	9.64 [9.60]	27.50 [27.48]	9.45 [9.43]

¹H NMR spectra of Schiff base:

The ¹H NMR Spectrum of ligand shows singlet for 1H at $\delta=10.93$ ppm (pyridine ring cotaining -OH), singlet for 2H of phenolic -OH at $\delta=5.35$ ppm, singlet for 2H (azomethinic proton) at $\delta=9.85$ ppm [15]. The signals of seven aromatic protons observed in the range of $\delta=7.26$ -7.68 ppm [16,17].

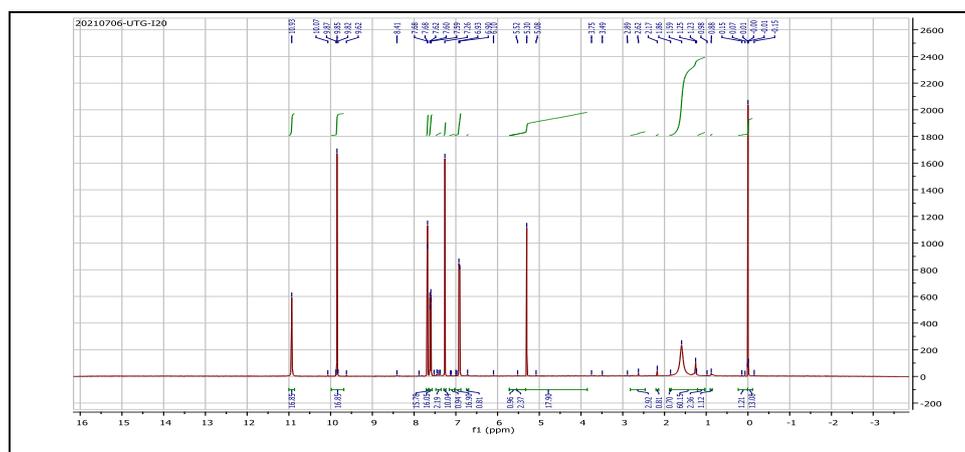


Fig.1. ¹H NMR spectrum of Schiff base ligand (HPMBP).

¹³C NMR spectra of Schiff base:

The ^{13}C NMR of the Schiff base ligand i.e. 2,2'-(1E,1'E)-(6-hydroxypyrimidine-2,4-diyl)bis(azan-1-yl-1-ylidene) bis(methan-1-yl-1-ylidene)bis(4-bromophenol) was determined in CDCl_3 . Seven signals were observed in ^{13}C NMR Spectra in the range of $\delta = 195.32\text{--}111.24$ ppm. The peak observed at $\delta = 160.44$ ppm is due to azomethine ($-\text{CH}=\text{N}-$) carbon. The peaks observed at $\delta = 111.24\text{--}139.58$ ppm belong to the aromatic carbons of two phenyl ring. Peak observed at $\delta = 195$ ppm is of deshielded pyrimidine ring carbon due to conjugation effect of the electronegative nitrogen atom present in Schiff base [18]. The Peak observed at $\delta = 135.51$ ppm may be attributed to pyrimidine ring aromatic carbons.

Mass spectrum of Schiff base:

Mass spectra is a important tools to ensure the purity of prepared Schiff base ligand (HPMBP) as well as depict their characteristic fragmentation and expected molecular weight. The mass spectrum of ligand (HPMBP) shows a peak at $m/z = 491.95$ (M^+ Peak) which confirms the formation of Schiff base (HPMBP).

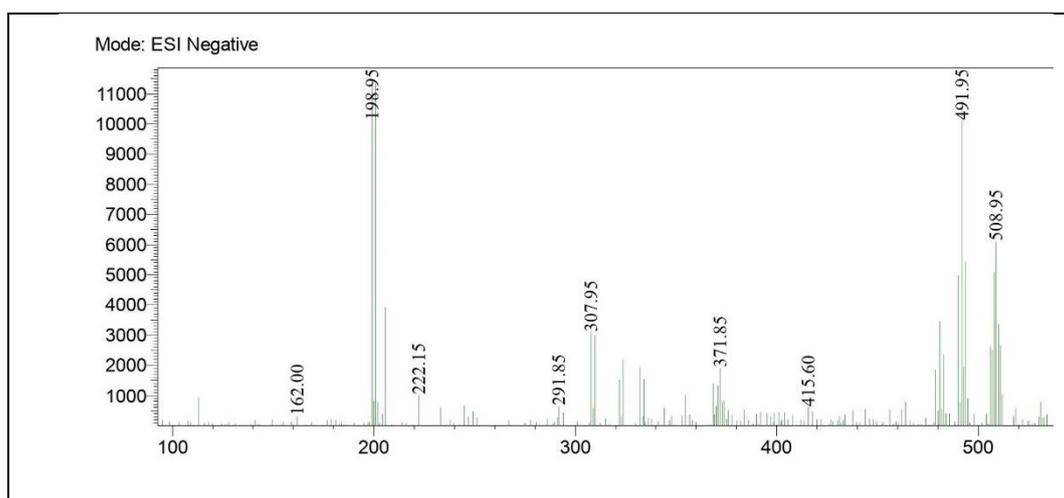


Fig.2. Mass spectrum of Schiff base ligand (HPMBP).

FT-IR analysis

The FT-IR spectral data of ligand (HPMBP) and their metal complexes were recorded and summarized in table no.2. The FT-IR spectra of the metal complexes were analysed and compared with Schiff base ligand for elucidate the involvement of the coordination sites in chelation. The characteristics peaks in the FT-IR spectra of the Schiff base ligand and its metal complexes were considered and compared. The FT-IR spectral data of ligand (HPMBP) and its metal complexes were compared to confirm the changes during formation of complexes. Spectra of Schiff base ligand exhibited the characteristics band at 3475 cm^{-1} is due to phenolic $-\text{OH}$ of ligand and in metal complexes the band at 3475 cm^{-1} is missing, it indicates that $-\text{OH}$ is engaged in bonding with metal [19]. In complexation, the $-\text{HC}=\text{N}-$

band shifts to lower wave numbers compared to the ligand, indicating that the nitrogen atom of the azomethine group is coordinated to the metal ion. The band of weak intensity observed in metal complexes in the region $506-527\text{ cm}^{-1}$ is assigned to M-O bond stretching frequency and in the region of $456-512\text{ cm}^{-1}$ is assigned to the M-N bond stretching frequency [20]. From above confirmative FT-IR spectral data it is clear that two azomethine nitrogen -HC=N- and two phenolic hydroxyl -OH group take part in the coordination with metal ion [21,22].

Table 2: FTIR spectral data of the ligand (HPMBP).and its metal complexes (cm^{-1}).

Ligand/Metal Complexes	$\nu(2\text{-OH})$ phenolic - OH	$\nu(-\text{OH})$ pyrimidine ring -OH	$\nu(\text{C}=\text{N})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
HPMBP	3545	3413	1659	--	--
[Ni(II)L]	--	3414	1616	506	488
[Cu(II) L(H ₂ O) ₂]	--	3414	1625	564	478
[Co (II) L(H ₂ O) ₂]	--	3415	1648	527	456
[Zn(II) L]. 2H ₂ O	--	3412	1634	524	455
Mn(II) L(H ₂ O) ₂]	--	3413	1637	482	451

Powder X-ray diffraction

The P-XRD of metal complexes were scanned at wave length 1.540 \AA in range $2\theta = 20-80^\circ$.

The strong and broad peaks indicate the formation of the metal complexes, the presence of large, weak peaks suggests a microcrystalline structure [23]. The P-XRD data is useful for determination of lattice parameters, cell parameters, crystal system etc. are given in table no.4. The P-XRD pattern shows the crystalline nature of transition metal complexes [24].

Table 3: XRD spectral data of Metal complexes.

Complexes	[Ni(II) L[[Cu(II)L(H ₂ O) ₂]	[Co(II)L(H ₂ O) ₂]	[Zn(II)L].2H ₂ O	[Mn(II)L(H ₂ O) ₂]
No. of reflection	12	15	17	22	13
maxima(2θ)	19.318°	17.131°	11.862°	53.165°	11.710°
Intensity	16383.02 a.u.	12066.59 a.u.	1937.16 a.u.	1042.36 a.u.	15506.38 a.u.
d value	4.59100 \AA	5.17187 \AA .	7.45478 \AA .	$1.72\text{ }140\text{ \AA}$.	7.55119 \AA .
Lattice constants	$a = 14.852\text{ \AA}$, $b = 9.121\text{ \AA}$,	$a = 13.257\text{ \AA}$, $b = 11.235\text{ \AA}$,	$a = 10.659\text{ \AA}$,	$a = 6.870\text{ \AA}$. $B = 9.820\text{ \AA}$.	$A = 16.239\text{ \AA}$. $b = 8.610\text{ \AA}$.

	$c = 8.129 \text{ \AA}$	$c = 15.942 \text{ \AA}$,	$b = 9.369 \text{ \AA}$, $c = 8.283 \text{ \AA}$	$C = 12.640 \text{ \AA}$.	$C = 6.294 \text{ \AA}$.
Unit cell volume	947.45 \AA^3	2370.60 \AA^3	800.11 \AA^3 .	748.79 \AA^3 .	879.40 \AA^3 .
Crystal Size	72.36 \AA	190.40 \AA	107.14 \AA	153.45 \AA	207.08 \AA
Axis and axis angle	$a \neq b \neq c$ and $\alpha = \gamma = 90^\circ \neq \beta$	$a \neq b \neq c$ and $\alpha = \beta = \gamma = 90^\circ$	$a \neq b \neq c$ and $\alpha = \gamma = 90^\circ \neq \beta$	$a \neq b \neq c$ and $\alpha = \gamma = 90^\circ \neq \beta$	$a \neq b \neq c$ and $\alpha = \gamma = 90^\circ \neq \beta$
Crystal system	Monoclinic	Orthorombic	Monoclinic	Monoclinic	Monoclinic

Thermal analysis

The thermal stability of Schiff base ligand and its complexes have been checked by thermogravimetric analysis in temperature range from 0-1000 °C under a nitrogen atmosphere. The TGA curve of the Ni(II) complex show no mass loss up to 350 °C reveals that the absence of lattice and coordinated water. At the temperature range 350-550 °C mass loss represent the removal of non coordinated part of ligand, At the temperature range 550 to 750 °C broad endothermic peak was observed may be attributed to mass loss represent the decomposition of coordinated part of ligand. Above 750 °C temperature stable nickel oxide was obtained [25]. The TGA curve of Zn(II) complex shows loss of lattice water in the temperature range 0- 100°C . The temperature range 100-670 °C mass loss observed due to decomposition of ligand. In final step stable zinc oxide was formed. The thermograms of Cu[II], Co(II), and Mn(II) metal complexes shows same pattern of decomposition. In first step coordinated mass loss at 200-400 °C temperature range is attribute to elimination of two coordinated water molecule. After this temperature range 400-700 °C mass loss is represent the ligand prrolysis [26]. Finally above 750 °C temperature residue of stable oxides of Cu[II], Co(II) and Mn(II) was formed [27,28]

Antimicrobial activities:

The Schiff base ligand and its transition metal complexes were screened against antifungal and antibacterial strain. All these synthesized complexes were found bioactive. The observation showed that the transition metal complexes are more bioactive than the Schiff base ligand (HPMBP) [29]. Activity variation of ligand and complexes depends on the permeability of the cell membrane, chelation and type of ligand donor atoms [30,31]

Table 4. Recommended values consider:

R (Resistant)	Intermediate sensitive	Sensitive	Highly Sensitive
Upto 8 mm	> 8 to 12 mm	>12-18 mm	≥ 18 mm

Antibacterial activity:

The bio-efficiency of synthesized Schiff base ligand and its transition metal complexes have been tested against one gram positive bacterial strain i.e *Staphylococcus aureus* and two gram negative bacterial strain i.e *Pseudomonas aeruginosa* and *Klebsiella pneumonia*. The antibacterial activity of ligand and its complexes screened by using disc diffusion method. The result showed that metal complexes exposed the good and effective inhibitory effect on the growth of bacteria than Schiff base ligand, but some complexes are non effective [32]. Cu(II) complex on *Staphylococcus aureus* (+) and *Pseudomonas aeruginosa* (-) bacterial strain shows good result of antimicrobial activity than Schiff base ligand because of their chelation capability [33]. The antibacterial activity data are summarized in table 5.

Table 5. Antibacterial activity of Schiff base ligands (HPMBP) and metal complexes series

Sample No.	<i>Staphylococcus aureus</i> (+)	<i>Pseudomonas aeruginosa</i> (-)	<i>Klebsiella pneumonia</i> (-)
Control	-ve	-ve	-ve
HPMBP	R	R	R
[Ni(II)L]	R	28.5	R
[Cu(II) L(H ₂ O) ₂]	21.5	10	R
[Co (II) L(H ₂ O) ₂]	R	R	18.5
[Zn(II) L]. 2H ₂ O	R	R	R
Mn(II) L(H ₂ O) ₂]	R	R	35

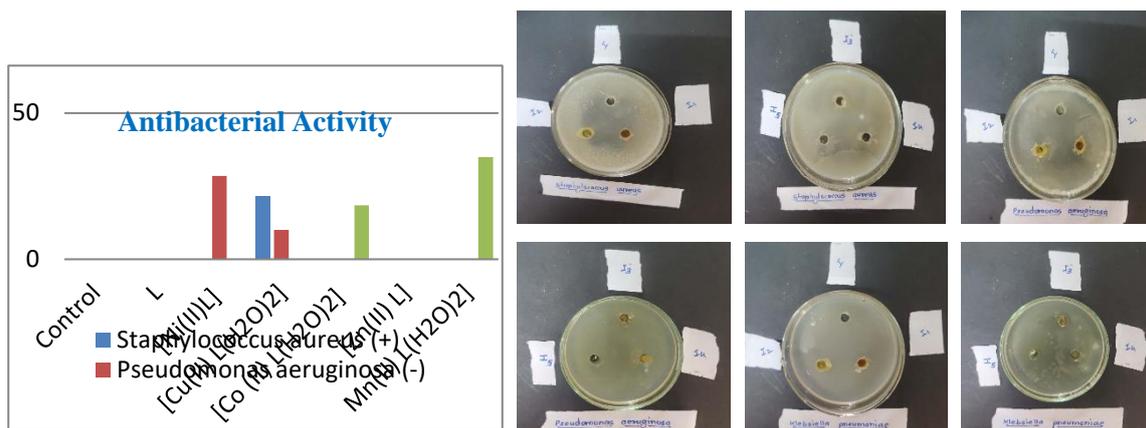


Fig.3 Inhibition zones formed for (a) *S. aureus* (b) *P. aeruginosa* (c) *K. pneumoniae*

Antifungal activity:

The antifungal activity of prepared compound was evaluated by disc diffusion method [34]. The Schiff base ligand and their metal complexes were tested against four fungal strains i.e. *Penicillium chrysogenum*, *Trichoderma viride*, *Aspergillus niger* and *Candida albicans* Fungi. The antifungal screening result exposed that Schiff base ligand and its all the metal complexes showed highly sensitive against *Penicillium chrysogenum*, *Aspergillus niger* and *Candida albicans*. However, they show inferior fungal activity against *Trichoderma viride*. The superior antifungal activity proved that the presence of azomethine group in ligand and metal complexes for their potential use in the region of medicinal bio-inorganic chemistry [35]. The antifungal activity data is given in table 6.

Table 6. Antifungal activity of Schiff base ligands (HPMBP) and metal complexes series

Sample No.	<i>Penicillium chrysogenum</i>	<i>Trichoderma viride</i>	<i>Aspergillus niger</i>	<i>Candida albicans</i>
Control	-ve	-ve	-ve	-ve
HPMBP	30	R	30	40
[Ni(II)L]	30	R	30	40
[Cu(II) L(H ₂ O) ₂]	30	R	35	30
[Co (II) L(H ₂ O) ₂]	30	R	35	35
[Zn(II) L]. 2H ₂ O	30	R	35	23
Mn(II) L(H ₂ O) ₂]	30	R	35	40

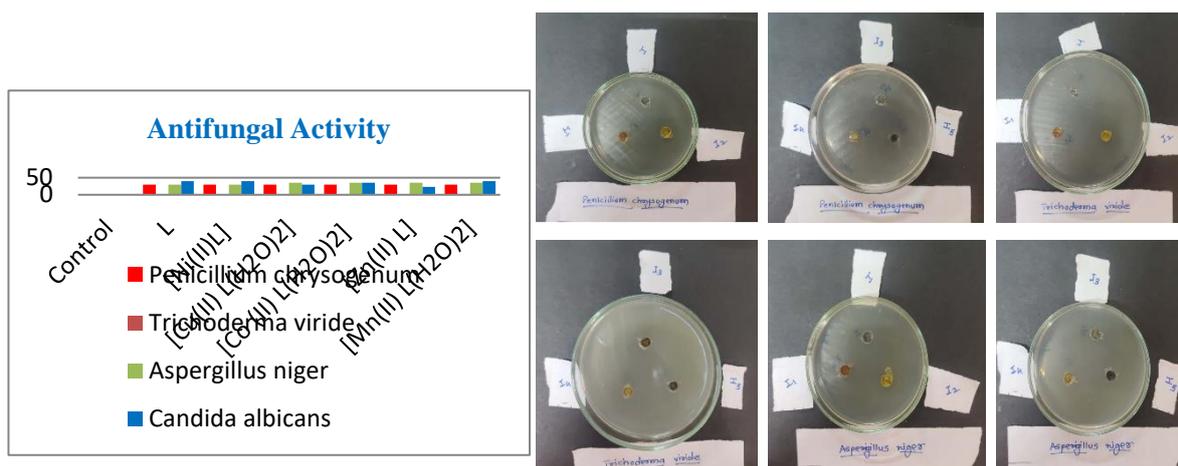


Fig.4 Inhibition zones formed for (a) *P.chrysogenum*, (b) *A.niger* (c) *C.albicans* (d) *T.viride*

CONCLUSION:

In this article, coordination chemistry of 2,2'-(1E,1'E)-(6-hydroxypyrimidine-2,4-diyl)bis(azan-1-yl-1-ylidene)bis (methan-1-yl-1-ylidene)bis(4-bromo phenol) (HPMBP) Schiff base ligand was described. The characterization confirmed the composition and structure of ligand and its metal complexes. From spectral data it was observed that Ni(II) and Zn(II) complexes having tetrahedral structure while Cu(II), Co(II) and Mn (II) having octahedral structure. The Schiff base ligand coordinates to metal through azomethine nitrogen and phenolic -OH of Schiff base ligand (HPMBP). P-XRD data suggest monoclinic crystal system for Ni[II], Co[II], Zn[II] and Mn[II] metal complexes and orthorhombic crystal system for Cu[II] complex. The biological activity screening showed that the transition metal complexes are more bioactive than the Schiff base ligand.

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