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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF METAL SCHIFF BASE COMPLEXES DERIVED FROM PYRROLE-2-CARBALDEHYDE

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ABSTRACT: Synthesis of a new N-((1H-pyrrol-2-yl)methylene)-4-methylaniline(PMM) Schiff base derived from Pyrrole-2-carbaldehyde and p-toluidine and its coordination with compounds Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Zr(IV), Pd(II) and Ag(I) are described. The ligand and complexes have been characterized on the basis of spectral analysis. Antibacterial and antifungal activities of ligand and its metal complexes have been screened for various human pathogenic bacteria and fungus.

KEYWORDS: Schiff base,Pyrrole-2-carbaldehyde, p-toluidine,antibacterial, *Aspergillus flavus.*

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1.INTRODUCTION

Compounds with the structure of -C=N- (azomethine group) are known as Schiff bases, which are usually synthesized from the condensation of primary amines with compounds having active carbonyl groups [1]. The biological activities of Schiff bases have attracted considerable attention to organic and medicinal researchers for many years. Schiff bases are now well known for their importance in biological fields such as anticancer [2], antimicrobial [3,4], anti-inflammatory [5,6], antiviral [7], analgesic [8], pesticidal [9], and antioxidant [10,11] agents. Related to anti-inflammatory effects, it was reported that several Schiff bases with pyrazole, thiazole, thiazoline and benzothiazole moiety and their metal complexes with Cu(II), Ni(II), and Zn(II) [12-14] posses important anti-inflammatory effects. These compounds inhibit the activity of cyclooxygenase

(COX) and 5- lipooxygenase enzymes [15,16], and they can also scavenge the free radicals, being known by the implication of the free radicals and oxidative stress in inflammatory diseases [17,18]. At the same time it was noted that the low levels of magnesium are associated with the inflammation and, as a result, a large number of magnesium complexes have been synthesized and their anti-inflammatory effects were studied [19]. Based on the aforementioned applications of Schiff bases, this study presents synthesis, characterization and antimicrobial effects of new Schiff bases and their complexes with Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Zr(IV), Pd(II) and Ag(I).

2. MATERIALS AND METHODS

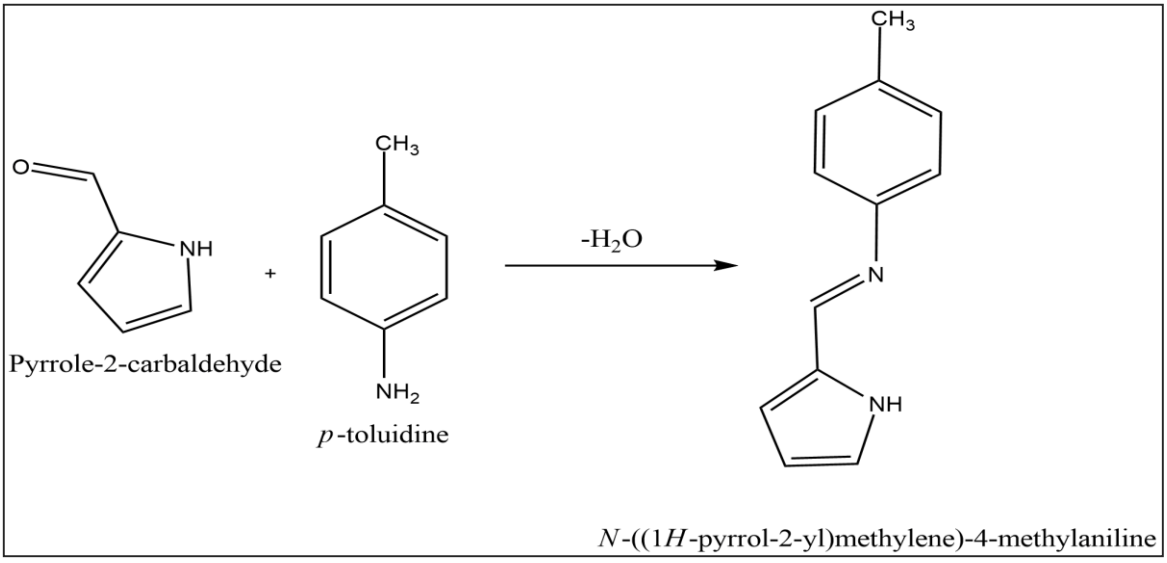
The chemicals and solvents used in this work were of Analar grade. All the glass wares used were washed thoroughly with distilled water and dried in an oven.

Infrared Spectrophotometric Measurement*:* The infrared spectra of all complexes were recorded in KBr disc on a Shimadzu double beam infrared spectrophotometer and measuring the relative intensity of transmitted light energy versus wave number in the region of 4000-400 cm^{-1}.

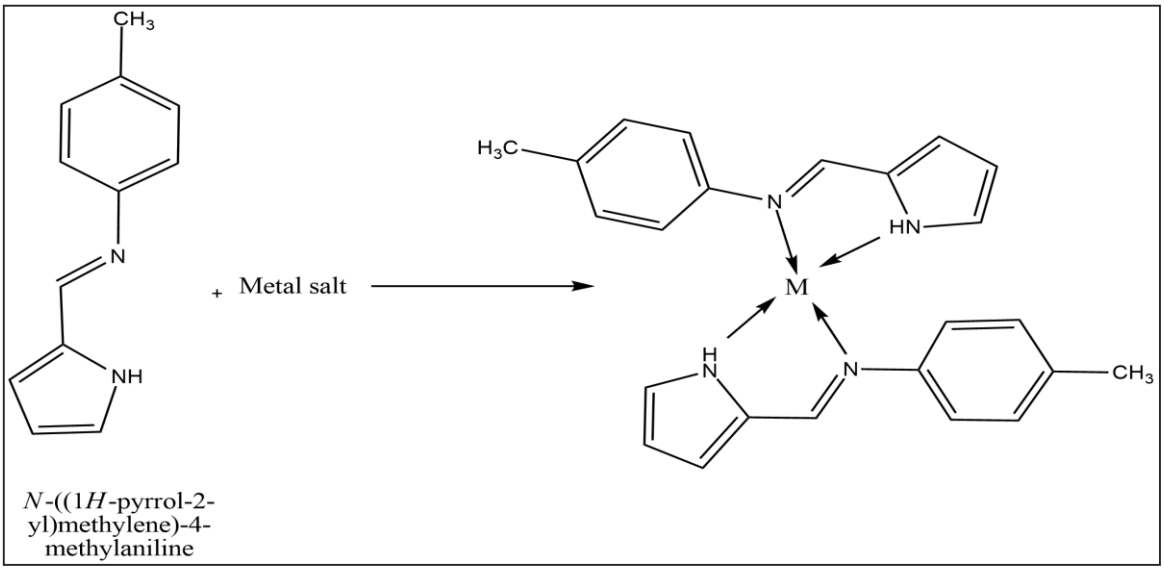
^{1}H-NMR Spectrometric Measurement*:* The proton NMR spectra of the ligandand complexes were recorded using acetone as a solventin Brucker EXT40178, 400MHz NMR spectrometer.

Synthesis of N-((1H-pyrrol-2-yl)methylene)-4-methylaniline(PMM)Schiff base (Scheme I): Schiff base was prepared by condensation of pyrrol-2-carbaldehyde(0.01mol)with p-toluidine (0.01 mol)in alcoholic medium and the mixture was refluxed for 4-5 hours at 50-60 ºC.After checking with TLC ,the resultant product was recrystallized with ethanol and taken for further characterization.

Synthesis of metal complexes (Scheme II): Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Zr(IV), Pd(II) and Ag(I) complexes were prepared by the addition of alcoholic solution of metal salt(0.005 mol) and the ligandN-((1H-pyrrol-2-yl)methylene)-4-methylaniline(0.01 mol**)**.The mixture was then refluxed for 4-5 hours.On cooling solid complexes were precipitated out which were filtered ,washed with cold ethanol and dried in a vacuum desiccators over fused $CaCl_2$



Scheme I: Synthesis of N-((1H-pyrrol-2-yl)methylene)-4-methylaniline(PMM)schiff base



Scheme II: Synthesis of metal complexes from Schiff base

Assay of Antibacterial Activity: Antibacterial activity was determined by disc diffusion method as described by Bauer*et al*., 1966 [20]. By inoculating a loopful of strain in Mueller Hinton broth separately and incubated at 37°C on a rotary shaker for 12 hrs. Then 0.1 ml of fresh inoculum (containing around 1 - 2 × 10^6 CFU/ml as per McFarland standards) was spread onto the surface of sterile Mueller Hinton agar plates using a sterilized spreader. Then discs impregnated with compounds (1mg/disc) and solvent controls were placed on plates with the help of a sterilized forceps and the plates were incubated aerobically at 37°C. Similarly a negative solvent control (DMSO) disc were placed on each pathogen inoculated plates. The entire microbial assay was carried out under strict aseptic conditions. The zone of inhibition (mm) of the different metals was examined after 12-18 hrs.

Assay of Antifungal Activity: Antifungal activity test was carried out following the modification of the method originally described by Bauer *et al.,* (1966) [20]. Potato Dextrose Agar (PDA) was prepared and autoclaved at 15 lbs pressure for 20 minutes and cooled to 45ºC. The cooled media was added 10ml/L tartaric acid (10%) act as antibacterial agents and poured on to sterile petriplates and allowed for solidification. The plates with media were seeded with the respective microbial suspension using sterile swab. The various solvents extract prepared discs individually were placed on the each petriplates and also placed control and standard (Amphotericin B (100 Units/ Discs)) discs. The plates were incubated at 28ºC for 72 hrs. After incubation period, the diameter of the zone formed around the paper disc were measured and expressed in mm.

3. RESULTS AND DISCUSSION

Spectral studies: The interaction between metal ions and N-((1H-pyrrol-2-yl)methylene)-4-methylaniline (PMM), yielded the desired complexes.

3.1.FT-IR spectra: The IR spectra [Table 1] of the metal complexes show bands in the region 1616-1658 cm^{-1} which are assigned to υ(C=N) stretching vibration,which indicate the presence of azomethine group[21, 22]. The band in the region 1396 - 1452 cm^{-1} corresponds to υ(C=C) stretching vibration due to phenyl group, indicating the coordination of N-((1H-pyrrol-2-yl)methylene)-4-methylaniline(PMM)schiff base to the metal ions. The bands within 450 - 482 $cm^{-1}$are assigned to υ(M—N) stretching vibrations, respectively [23,24]. These bands confirmed the coordination of the schiff base to the metal ions.

Table.1: IR Spectral data (cm^{-1})of ligand and their metal complexes

S.No	Compound	Frequency(cm^{-1})		
		υ(C=N)	υ(C=C)	υ(M-N)
1	N-((1H-pyrrol-2-yl)methylene)-4-methylaniline (PMM)	1618	1417	-
2	$[Mn(PMM))_2]Cl_2.4H_2O$	1616	1415	482
3	$[Fe(PMM)_2]Cl_2.6H_2O$	1637	1400	480
4	$[Co(PMM)_2]Cl_2.6H_2O$	1620	1419	453
5	$[Ni(PMM)_2]Cl_2.6H_2O$	1622	1427	457
6	$[Cu(PMM)_2]Cl_2.2H_2O$	1654	1396	453
7	$[Zn(PMM)_2]Cl_2$	1658	1452	450
8	$[Zr(PMM)_2]OCl_2.8H_2O$	1656	1446	459
9	$[Pd(PMM)_2]Cl_2$	1656	1450	457
10	$[Ag(PMM)_2]NO_3$	1634	1457	458

IR spectrum of Schiff base shown in Fig.1, showed the band region 1618 cm^{-1}, which indicate the presence of υ(C=N) stretching vibration. The coordination of the azomethine further confirmed by the appearance of non-ligand bands at 482, 480, 453, 453, 450, 459, 457 cm^{-1} due to υ(M—N) [25-30]. IR spectrum of Fe complex shown in Fig.2.

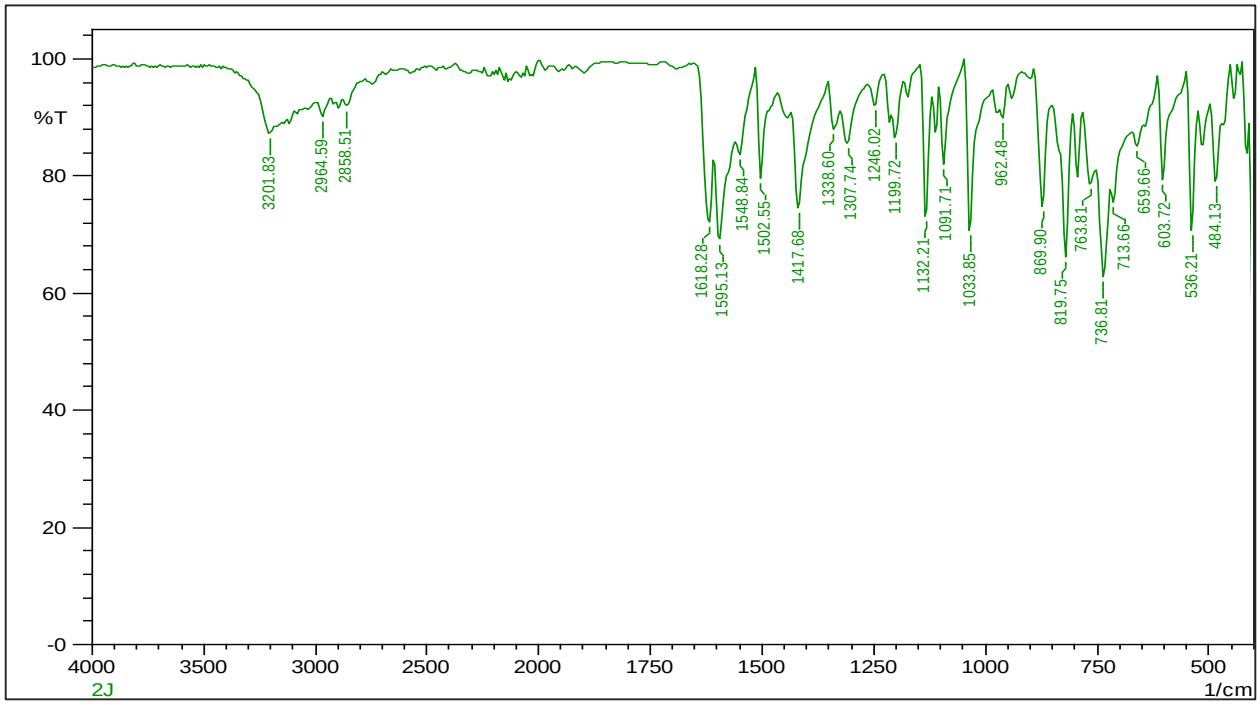


Fig.1: IR spectrum of N-((1H-pyrrol-2-yl)methylene)-4-methylaniline (PMM)Schiff base

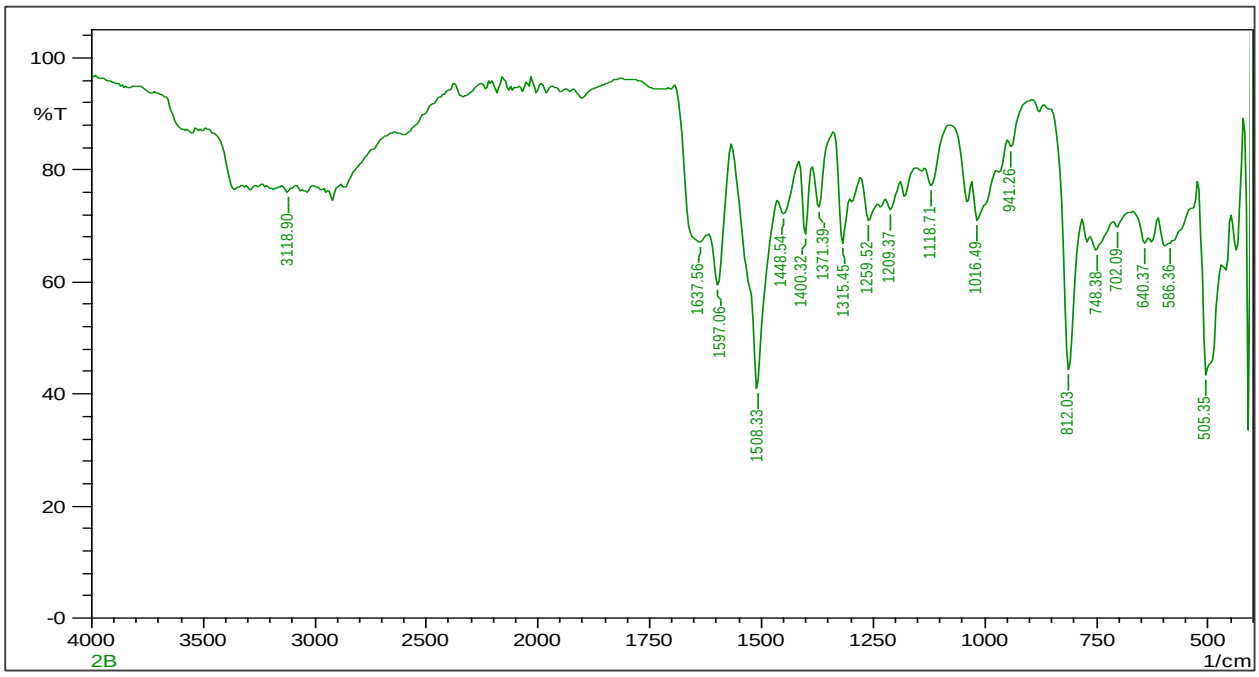


Fig.2: IR spectrum of $[Fe(PMM)_2]Cl_2.6H_2O$complex

3.2.^{1}H NMR spectra

The ^{1}H NMR spectrum of the Schiff base (Fig.3) exhibits a multiple at 8.333-7.065ppm (m, Ar-H).Themultiplet at lowest field in the ^{1}H NMR spectrum (between δ 7.065- 7.165ppm), showing cross-peaks. This multiplet shows a cross-peak in the ^{1}H-^{1}H-COSY (Fig.5) with protons located in a multiplet at δ 7.1 -7.2ppm.

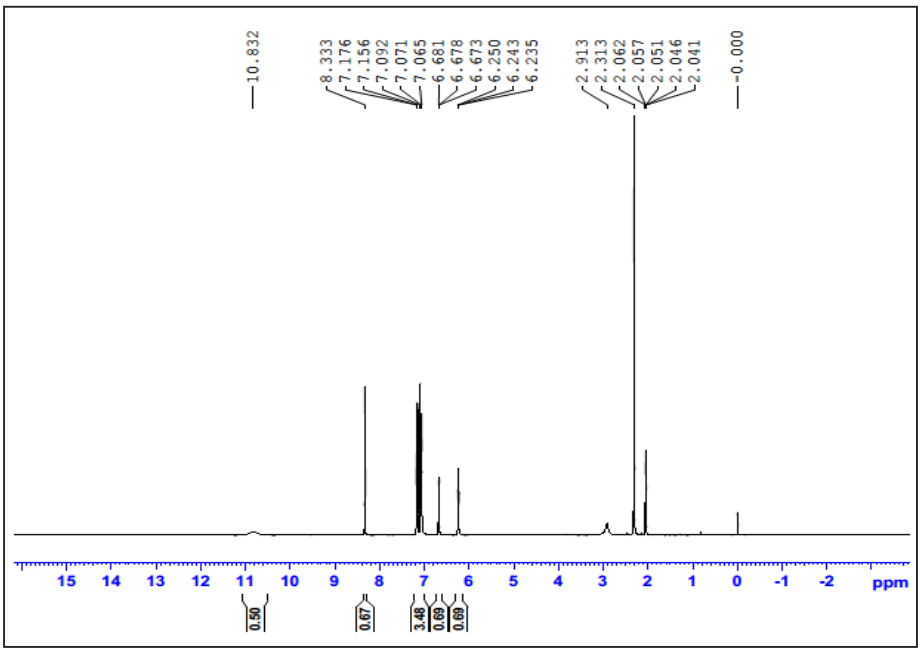


Fig.3: .^{1}H NMR spectrum of N-((1H-pyrrol-2-yl)methylene)-4-methylaniline (PMM) Schiff base

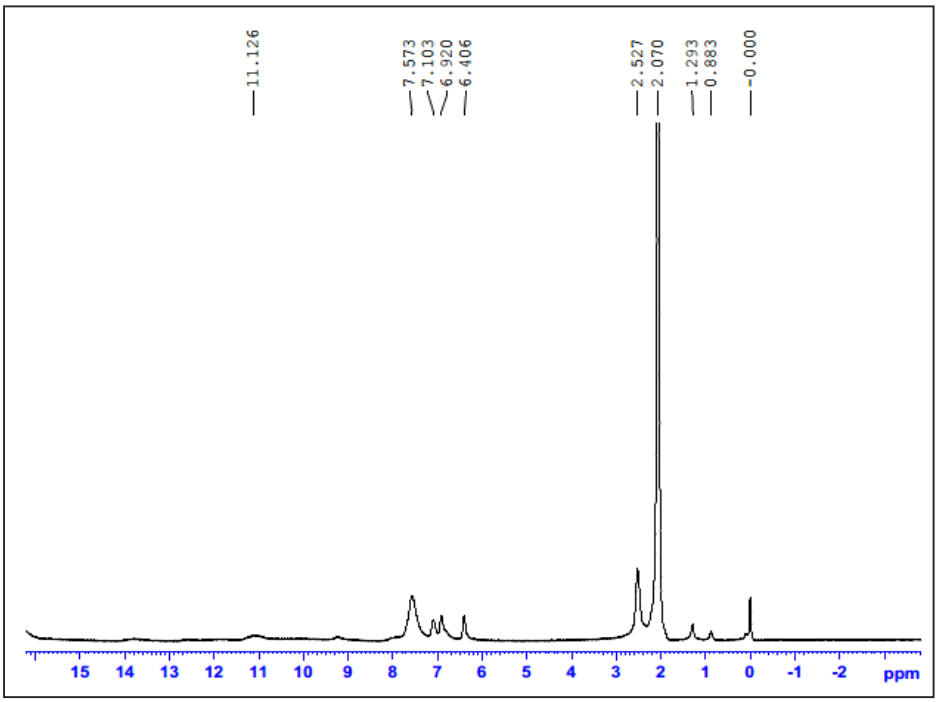


Fig.4: .^{1}H NMR spectrumof [Fe(PMM)$_2$]Cl$_2$.6H$_2$Ocomplex

3.3 ^{1}H-^{1}H-COSYspectrum

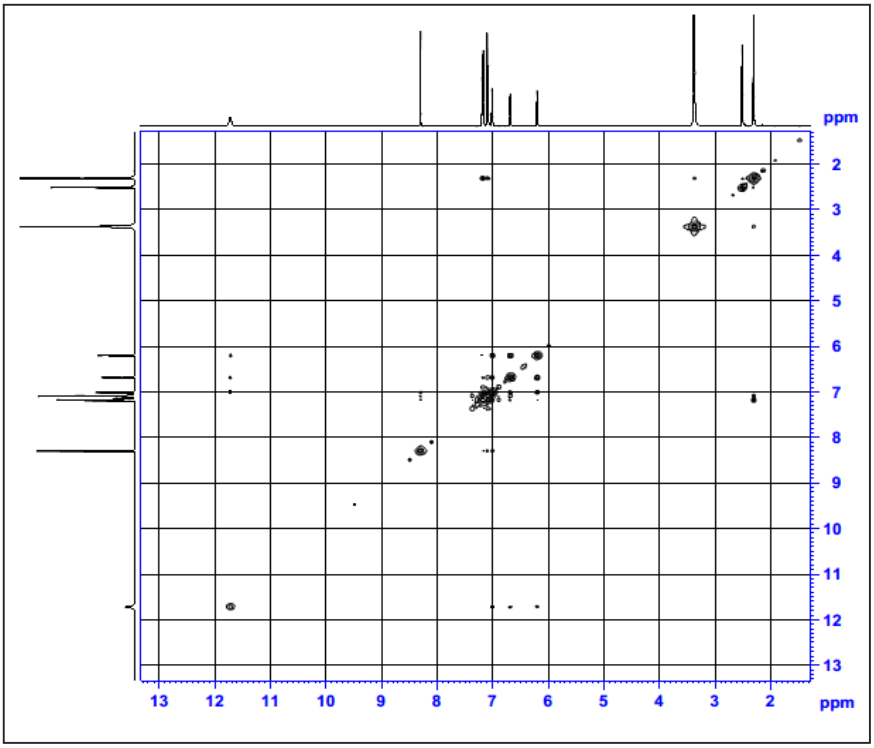


Fig.5: ^{1}H-^{1}H-COSYspectrum of N-((1H-pyrrol-2-yl)methylene)-4-methylaniline (PMM) Schiff base

3.4 Antimicrobial activity: The antibacterial activities of the Schiff base and metal complexes were tested against *Bacillus subtilis, Staphylococcus epidermis, Escherichia coli* and *Salmonella typhi* cultures. It can be seen that Fe, Ni, Cu and Zn complexes show antibacterial activity (Table 2,Fig 6).

Table 2: Assay of antibacterial activity against various human pathogen

Compound	***Bacillus subtilis***	***Staphylococcus epidermis***	***E. coli***	***Salmonella typhi***
$[Mn(PMM))_2]Cl_2.4H_2O$(a)	-	-	-	-
$[Fe(PMM)_2]Cl_2.6H_2O$(b)	-	4.0	2.6	10.0
$[Co(PMM)_2]Cl_2.6H_2O$ (c)	-	-	-	-
$[Ni(PMM)_2]Cl_2.6H_2O$(d)	3.0	4.0	-	7.0
$[Cu(PMM)_2]Cl_2.2H_2O$ (e)	1.0	-	-	3.0
$[Zn(PMM)_2]Cl_2$(f)	0.3	-	-	0.2
$[Zr(PMM)_2]OCl_2.8H_2O$ (g)	-	-	-	-
$[Pd(PMM)_2]Cl_2$(h)	-	-	-	-
$[Ag(PMM)_2]NO_3$(i)	-	-	-	-
Schiff base(PMM) (j)	-	-	-	-
Standard	15	20	25	21

Values are (Mean ± S.D)*; Zone of Inhibition in mm*

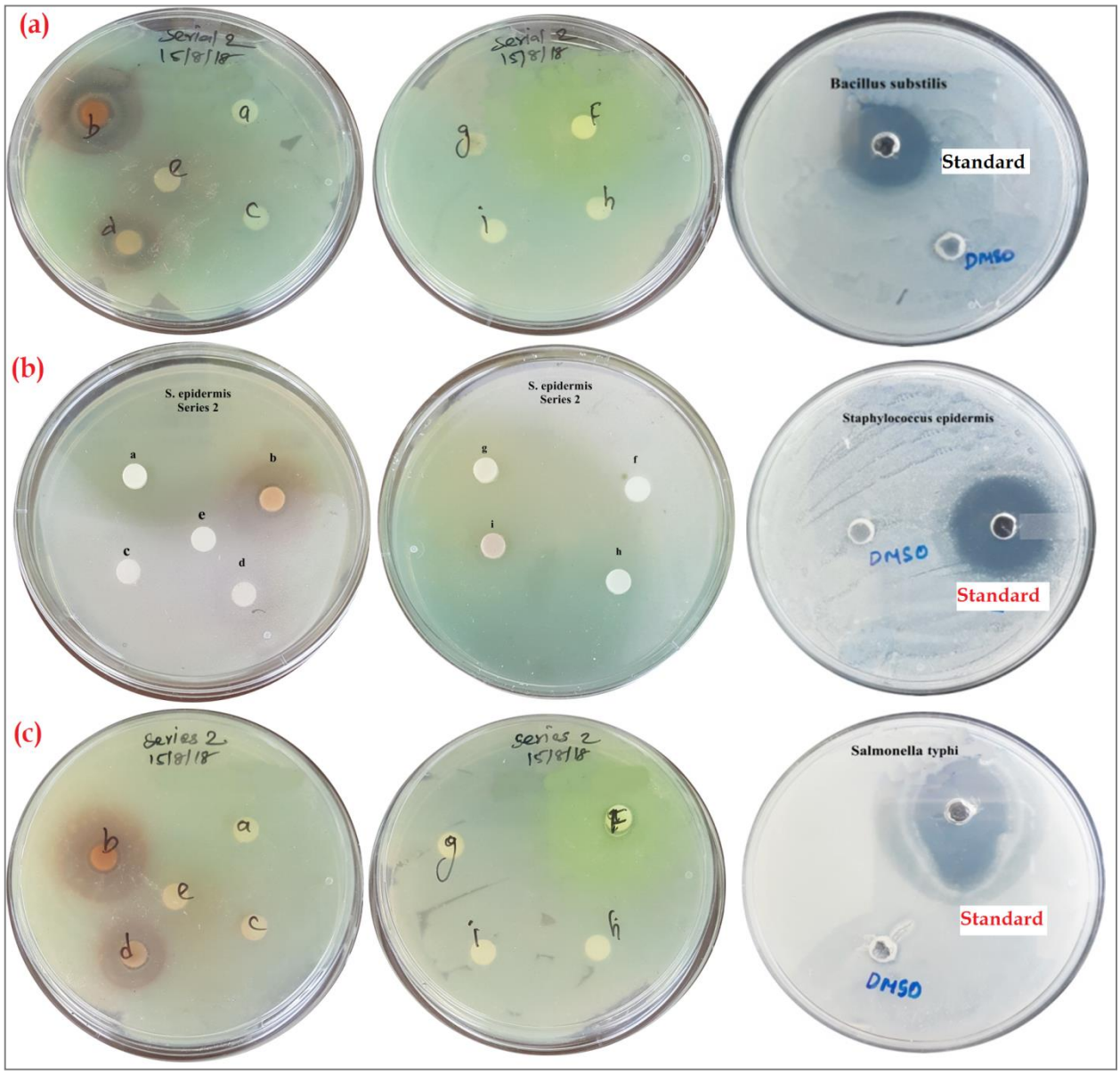


Fig. 6: Antibacterial activity of Schiff base and its metal complexes against *(a) Bacillus subtilis* (b) *Staphylococcus epidermis* and (c) *Salmonella typhi*

Antifungal activity

In the current study antifungal activity was obtained against *Aspergillus flavus.* Schiff base, Nickel and Zinc metal complexes showed more antifungal activity compared to other metal complexes (Table 3 & Fig.7).

Table 3: Assay of Antifugal Activity (*Aspergillus flavus*)

S. No.	Sample	Zone of Inhibition (mm in diameter)
1	Schiff base (PMM)	16
2	$[Mn(PMM))_2]Cl_2.4H_2O$	-
3	$[Fe(PMM)_2]Cl_2.6H_2O$	10
4	$[Co(PMM)_2]Cl_2.6H_2O$	-
5	$[Ni(PMM)_2]Cl_2.6H_2O$	18

6	$[Cu(PMM)_2]Cl_2.2H_2O$	07
7	$[Zn(PMM)_2]Cl_2$	22
8	$[Zr(PMM)_2]OCl_2.8H_2O$	-
9	$[Pd(PMM)_2]Cl_2$	-
10	$[Ag(PMM)_2]NO_3$	08
11	*Standard	14
12	Control	-

***Amphotericin B (100 Units/ Discs)**

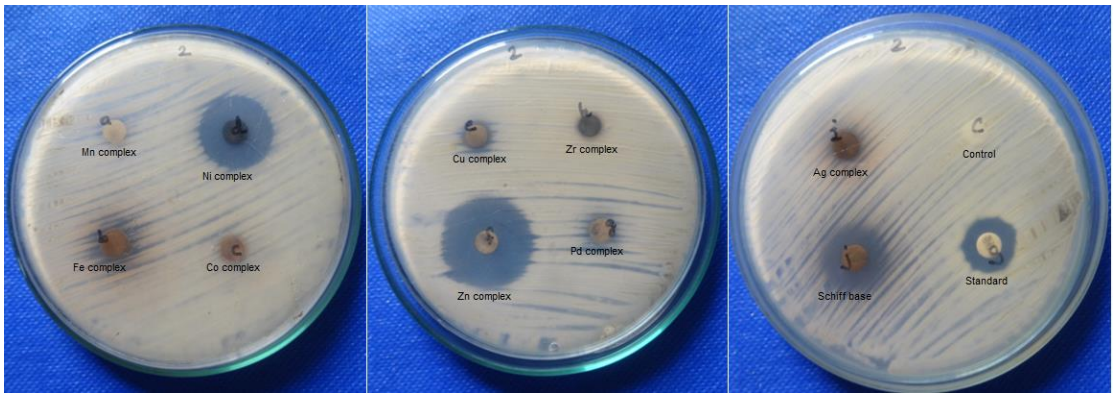


Fig. 7: Antifungal activity of Schiff base and its metal complexes against *Aspergillus flavus*

4. CONCLUSION

New Schiff base and their Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Zr(IV), Pd(II) and Ag(I) complexes have been synthesized and characterized using spectral methods (IR, ^{1}H-NMR). The schiff base and their metal complexes were screened for their antibacterial and antifungal activity against *Bacillus subtilis, Staphylococcus epidermis, Escherichia coli*, *Salmonella typhi* and *Aspergillus flavus*. From the results it can be seen that only Fe, Ni, Cu and Zn complexes showed antibacterial activity.Schiff bases and their Zn, Ni, Fe metal complexes showed significant antifungal activity.

CONFLICT OF INTEREST

There is no conflict of interest.

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