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3-(BENZO[D][1,3]DIOXOL-5-YL)-3-MORPHOLIN-4-YL-1-PHENYLPROPAN-1-ONE AND ITS METAL COMPLEXES: SYNTHESIS AND EXPLORATION OF THEIR BIOACTIVITY

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ABSTRACT

In the current scenario of research bio active metal complexes are gaining huge attention in medicinal organic chemistry. This research article is focused on the flourishing findings of bio activity of metal complexes with newly synthesized ligand. The synthesis, characterization and in vitro evaluation are studied for the metal complexes of 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one. The ligand was synthesized by reacting piperonal, morpholine and acetophenone. Various analytical (Chemical assays, TLC and Cyclic voltammetry) and spectral studies (FT-IR, UV-Visible, ^{1H} NMR, and ^{13}C NMR) were employed for the characterization of the ligand and its metal complexes.

KEYWORDS: Mannich Base, Morpholine Derivative, Piperonal, Bioactive Complexes, in Vitro Studies.

1. INTRODUCTION

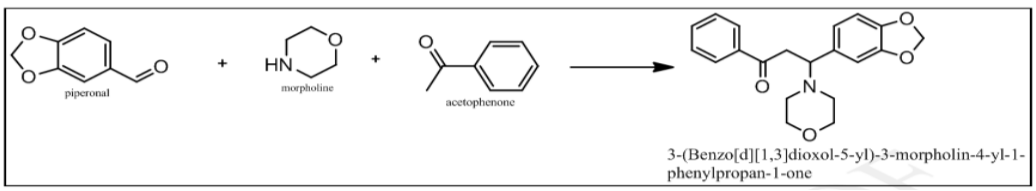
Mannich bases and their metal complexes are finding extensive applications in chemical and synthetic organic industries. They also exhibit a broad range of biological activities including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties.[1] The potentiality in biological activities of complexes is highly enhanced through the multidentate coordination behavior. Hence, the need for the synthesis of such complexes with a number of transition metals, characterization and in vitro

evaluations assume paramount importance in the field of medicinal organic chemistry[2,3,4,5]. Besides, Mannich base ligands have also been employed as catalysts in several reactions such as polymerization reaction, reduction of thionyl chloride, oxidation of organic compounds, reduction reaction of ketones, aldol reaction and epoxidation of alkenes.

The knowledge and clarity acquired through the literature survey motivated us to synthesis a new compound from the combination of piperonal, morpholine and acetophenone as they were not yet condensed for synthesizing Mannich base. Hence, our research article explores the synthesis, characterization and antimicrobial studies of a Mannich base, 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one and its complexes with a variety of transition metals such as Mn(II), Co(II), Ni(II), Cu(II) and Zn(II).

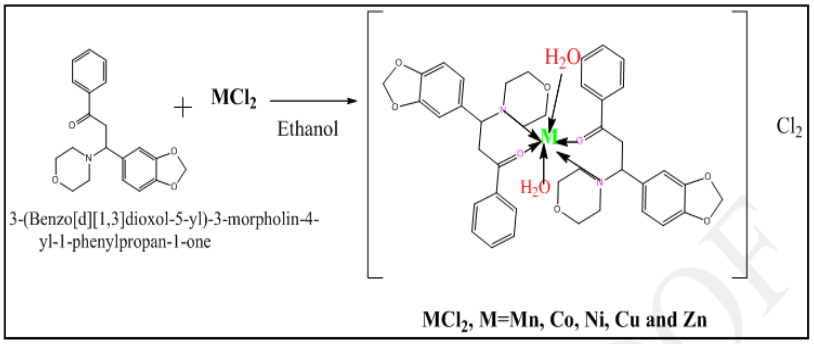
2. Experimental Methods: All the chemicals used were of AR grade and used without further purification unless otherwise stated. All the aromatic aldehydes were obtained from Avra Synthesis Pvt. Ltd., Hydrabad. Melting points of all the compounds were determined in open capillary tubes and are uncorrected. The homogeneity of compounds was checked by TLC on silica gel 'G' coated glass plates. IR spectra were recorded in KBr on Shimadzu FT-IR 8300 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 400 MHz in Bruker Advance II instrument using DMSO-d6 as medium and TMS as an internal standard. In vitro studies were carried out by disc diffusion method with proper incubation.

2.1 Synthesis of 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one (PMA): Piperonal, morpholine and acetophenone were taken in 1:1:1 ratio. 0.75 g of piperonal was taken in a round bottomed flask and 10 mL of ethanol was added. To this solution 0.5 mL of morpholine in ethanol was added and stirred well for 15 min by keeping the reaction mixture on a magnetic stirrer. The solution was made to alkali by adding NaOH pellets. To this solution 0.6 mL of acetophenone in ethanol was added and stirred. Stirring was continued under ice cold condition for about 2 h. The compound thus formed was filtered, washed and recrystallized using ethanol in hot condition (Scheme-1).



Scheme. 1: Synthesis of 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one.

2.2 Synthesis of transition metal complexes of 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one (M-PMA).



Scheme. 2: Synthesis of transition metal complexes of 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one (M-PMA).

A solution of 0.1 M of MCl_2 (M= Mn, Co, Ni, Cu and Zn) in methanol and 0.2 M of 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one in methanol were added to a round bottomed flask and stirred well using magnetic stirrer for an hour (Scheme-2). The complex formed was filtered, washed with distilled water and crystallized from absolute alcohol.

2.3 In vitro studies

In vitro studies for the 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one and its complexes were carried out by disk diffusion technique[6,7] against the test microorganisms such as *Staphylococcus aureus* (gram +ve), *Bacillus subtilis* (gram +ve), *Escherichia coli* (gram -ve), *Salmonella paratyphi* (gram -ve) and fungi *Candida albicans* and *Aspergillus niger*. *Ciproflaxacin* and *Chlotrimazole* were used as standards for antibacterial and antifungal studies respectively.

2.3.1 In vitro study -I

To study the capability of inhibition against the growth of pathogens, nutrient agar was used as a medium. This was prepared by dissolving 5 g of yeast extract, 10 g of meat extract, 5 g of peptone, 5 g sodium chloride and 20 g of agar in 100 mL of distilled water in a clean conical flask and the pH was maintained at 7. The solution was boiled to dissolve the medium completely and sterilized. After sterilization, 20 mL media was poured into the sterilized petri plates. These petri dish plates were kept at room temperature for an hour. Bacterial inocula containing approximately 10^5-10^6 CFU/mL was spread on the surface of the nutrient

agar. The recommended concentration of the test sample (100 mg/mL in DMSO) was introduced in the respective wells. Other wells supplemented with DMSO and standard antibacterial drug *Ciprofloxacin*. The plates were incubated at 37^{o}C for 24 h. During this period the test solution was diffused and affected the growth of the inoculated microorganisms. The capability of inhibition of samples was measured by measuring the diameter of inhibited zone that are developed in mm. The zone of inhibition values measured was presented in the Table-7 for comparing the potentiality of the compound and its complexes under study.

In order to clarify any participating role of DMSO in the bacterial screening, separate studies were carried out with pure solvent (DMSO) and showed no activity against any bacterial strains. In addition to this, a distinct study was also carried out against all the metal salt solutions individually. No appreciable activity was recorded by the individual metal ions.

2.3.2 In vitro study - II

The potato dextrose agar (PDA) was used as a medium for antifungal activity. The PDA was prepared by dissolving 20 g of potato extract, 20 g of agar and 20 g of dextrose in one liter of distilled water in a clean conical flask. The solution was boiled to dissolve the media completely and sterilized. After sterilization, 20 mL of media was poured into the sterilized petri plates. These petri plates were kept at room temperature for an hour to make the medium get solidified in plate. 0.5 mL of DMSO was used as solvent and 10 µg of *Clotrimazole* as control. It was also done by the same antibacterial activity procedure corresponding with antifungal drug *Clotrimazole* as standard. The zone of inhibition values measured was presented in Table-8 for comparing the potentiality of the compound and its complexes under study.

3. RESULTS AND DISCUSSION

3.1 Elemental Analysis

The molecular formula of the synthesized compound was proposed as $C_{20}H_{21}NO_4$, which was confirmed by the elemental analysis. The results of elemental analyses show 1:2 (metal: Ligand) stoichiometry for all the complexes with Mn, Co, Ni, Cu and Zn, which confirms the suggested general formula as $[C_{40}H_{46}N_2O_{10}M]Cl_2$. The analytical data of the ligand and their complexes are given in Table-1 and 1a. The presence of Chloride ion was confirmed by $AgNO_3$ test. The high molar conductance supports the electrolytic nature of metal complexes.[8,9]

Table. 1: Physical properties of PMA and its metal complexes M-PMA.

Compounds	Molecular formula	Molecular weight	Melting point / decomposition point	Conductance ($\Omega^{-1}cm^2mol^{-1}$in 10^{-3})
PMA	$C_{20}H_{21}NO_4$	339	170ºC	-
Mn(II)-PMA	$[C_{40}H_{46}N_2O_{10}Mn\ ]Cl_2$	868	178ºC	202
Co(II)-PMA	$[C_{40}H_{46}N_2O_{10}Co]Cl_2$	872	185ºC	180
Ni(II)-PMA	$[C_{40}H_{46}N_2O_{10}Ni]Cl_2$	871.6	176ºC	188
Cu(II)-PMA	$[C_{40}H_{46}N_2O_{10}Cu]Cl_2$	877	185ºC	160
Zn(II)-PMA	$[C_{40}H_{46}N_2O_{10}Zn]Cl_2$	878	312	165

Table. 1a: Elemental analysis of PMA and its metal complexes M-PMA.

Compounds	Molecular formula	Elemental analysis, % found (% Calculated)			
		C	H	N	O
PMA	$C_{20}H_{21}NO_4$	70.1 (70.7)	5.8 (6.2)	3.9 (4.1)	18.7 (19.0)
Mn(II)-PMA	$[C_{40}H_{46}N_2O_{10}Mn\ ]Cl_2$	54.8 (55.2)	4.9 (5.2)	2.9 (3.2)	18.2 (18.6)
Co(II)-PMA	$[C_{40}H_{46}N_2O_{10}Co]Cl_2$	54.8 (55.0)	4.8 (5.2)	2.9 (3.2)	17.9 (18.34)
Ni(II)-PMA	$[C_{40}H_{46}N_2O_{10}Ni]Cl_2$	54.6 (55.0)	4.8 (5.2)	2.9 (3.2)	17.5 (18.3)
Cu(II)-PMA	$[C_{40}H_{46}N_2O_{10}Cu]Cl_2$	54.0 (54.7)	4.7 (5.2)	2.9 (3.1)	17.5 (18.2)
Zn(II)-PMA	$[C_{40}H_{46}N_2O_{10}Zn]Cl_2$	54.3 (54.6)	4.9 (5.2)	2.8 (3.18)	17.5 (18.22)

3.2 FT-IR spectra

The structural relationship among the constituent atoms and group of the synthesized compound and its complexes were established using the data obtained from IR spectroscopy (Fig-1a – 1f). The mode of complex formation of complex was also clarified by the IR spectrum. IR frequencies corresponding to the respective vibrations are summarized in Table-2. The mode of coordination and its' sites were pointed out by comparing the IR spectrum of ligand and its complexes.

The normal νC-H of alkanes and aromatics are in the range of 3062-2561 cm^{-1}. The characteristic IR band observed at 3062 cm^{-1} is attributed to the νArC-H. The band appeared at 2920 cm^{-1} is assigned to νAliC-H. The νC=O was confirmed by the band observed at 1659 cm^{-1}. The νC=O of the ligand in complex was found lowered by ≈ 5 cm^{-1} from the spectrum of the ligand indicated the coordination of oxygen atom of carbonyl group of acetophenone with the metal ion. The νC-N-C of morpholine appeared at 1254 cm^{-1} in the spectrum of ligand has been found shifted to 10 to 12 cm^{-1} in spectrum of each complex suggesting the coordination is through N atom of morpholine. The bands due to νC-O-C and νC-H are retrieved in the spectra of the complexes when compared with their ligand spectrum. These changes have been further advocated by a medium intensity band observed in the range 532 cm^{-1} and 511 cm^{-1} for all the complexes are due to the νM-O and νM-N respectively [10,11,12].

IR data concludes that the free Mannich base is neutral bidentate and coordination occurs through O and N atoms of the ligand to the metal ions.

Table. 2: Characteristic IR bands (cm^{-1}) of PMA and its metal complexes.

Entry	Compound	Band assignment, cm^{-1}						
		υ Ar -H	υC=O	υC-N-C	υC-O-C	υM-N	υM-O	υH_2O
1.	PMA	3062	1659	1254	1103	---	----	---
2.	Mn-PMA	2999	1656	1244	1104	433	532	3312
3.	Co-PMA	3012	1656	1242	1106	431	518	3308
4.	Ni-PMA	3063	1659	1254	1104	415	517	3331
5.	Cu-PMA	3065	1655	1243	1104	427	522	3315
6.	Zn-PMA	3060	1657	1252	1107	414	523	3306

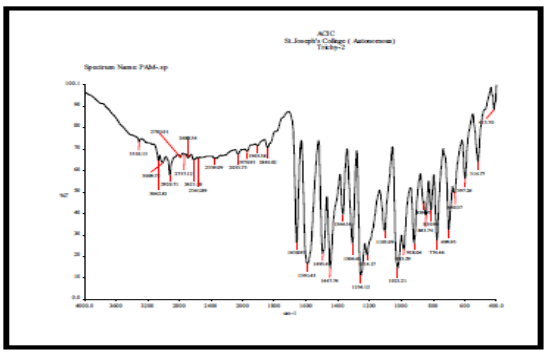


Figure -1a FT-IR spectra of PMA.

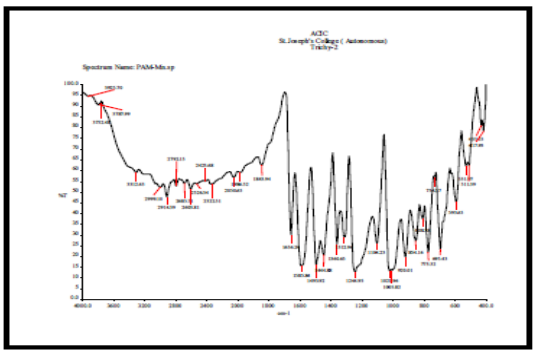


Figure -1b FT-IR spectra of Mn-PMA.

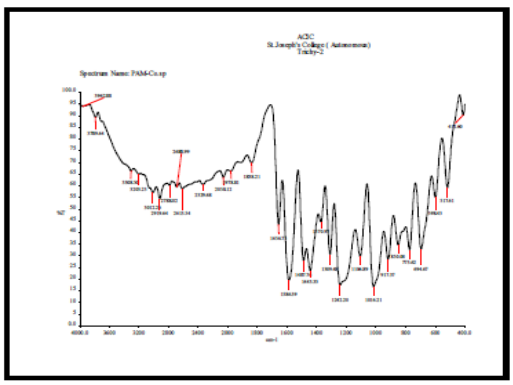


Figure -1c FT-IR spectra of Co-PMA.

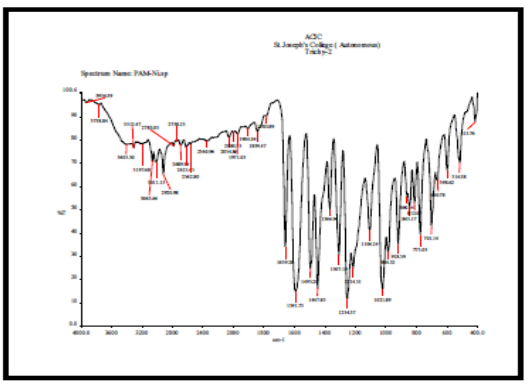


Figure -1d FT-IR spectra of Ni-PMA.

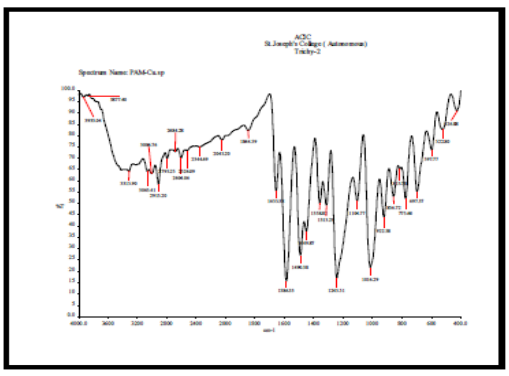


Figure -1e FT-IR spectra of Cu-PMA.

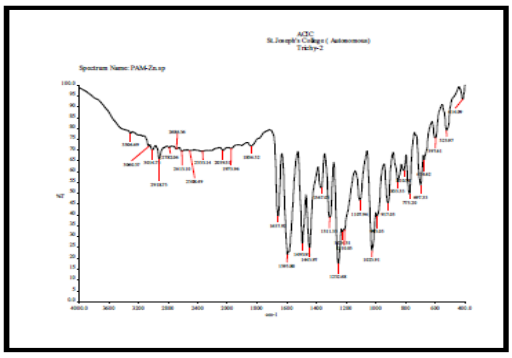


Figure -1f FT-IR spectra of Zn-PMA.

3.3 Electronic spectra

The Λ_{max} values of the compound and its complexes are adding still more evidences on the structural investigations (Fig-2a–2f). The electronic spectral measurements were used for assigning the structural relationships among the constituent groups of metal complexes based on the position and number of d-d transition peaks [7,8,9]. The electronic absorption spectra of PMA and its Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes were recorded at room temperature using 10^{-3}M DMSO solution of complexes and in the wavelength range of 250-900 nm. The intensity of absorption and its corresponding electronic transitions [13,14,15,16] are summarized in Table-3.

Table. 3: UV-Vis. Spectral and magnetic data of the pure ligand PMA and its metal complexes.

Entry	Compounds	Absorption		Transition	Magnetic moment (BM)	Geometry
		nm	cm^{-1}			
1.	PMA	258	38,759	-	-	-
		361	27,700			
2.	Mn (II)-PMA	259	38,610	$^6A_1g \rightarrow {}^4E_1g$,	5.92	Octahedral
		360	27,777	$^6A_1g \rightarrow {}^4T_2g$		
3.	Co (II)-PMA	258	38,759	$_4T_1g(F) \rightarrow {}_4T_2g(P)$	3.84	Octahedral
		267	37,453	$_4T_1g(F) \rightarrow {}_4A_2g(F)$		
		360	27,777	$_4T_1g \rightarrow {}_4T_2g(F)$		
4.	Ni (II)-PMA	258	38,759	$^3A_2g(F) \rightarrow {}^3T_1g(F)$	2.86	Octahedral
		361	27,700	$^33A_2g(F) \rightarrow {}^3T_1g(P)$		
5.	Cu (II)-PMA	362.9	27,548	$^2T_{2g} \rightarrow {}^2E_g$	2.74	Distorted Octahedral

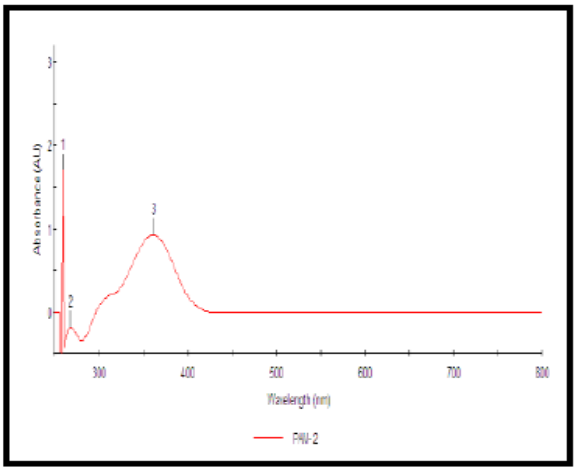


Figure -2a UV spectra of PMA.

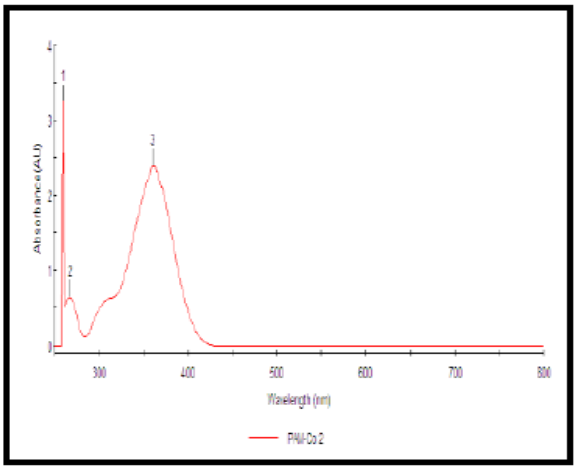


Figure -2b UV spectra of Co-PMA.

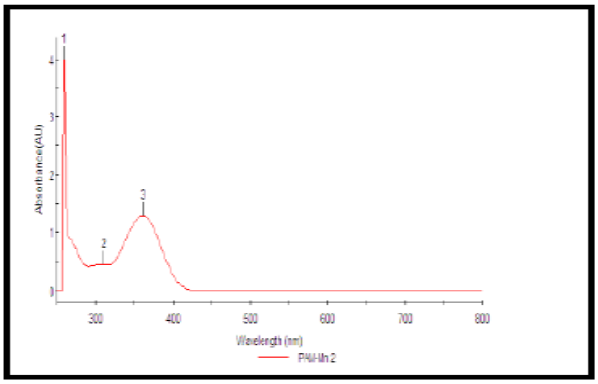


Figure -2c UV spectra of Mn-PMA.

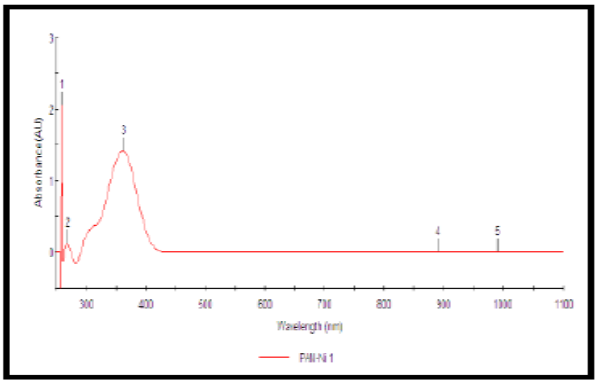


Figure -2d UV spectra of Ni-PMA.

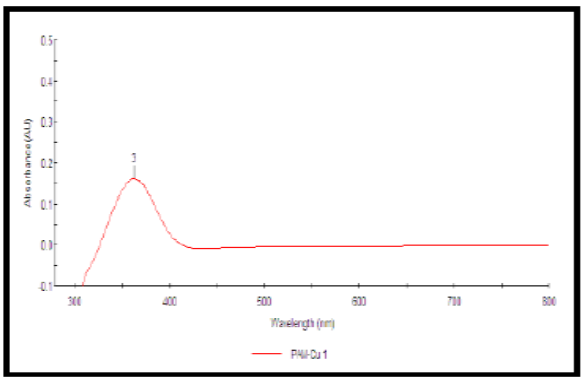


Figure -2e UV spectra of Cu-PMA.

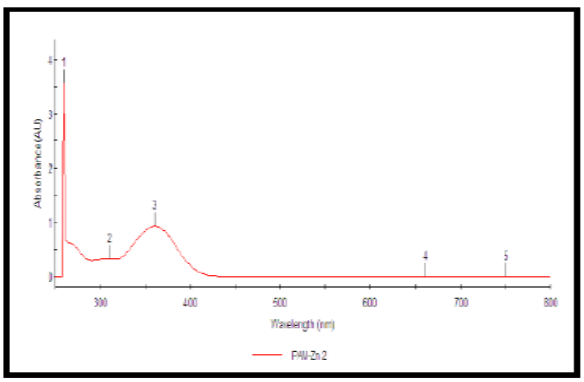


Figure -2f UV spectra of Zn-PMA

3.4 ^{1}H NMR spectra: The results obtained from ^{1}H NMR spectrum, recorded at VIT, Vellore using Bruker 400 MHz instrument, helped to find out the number of protons and their chemical environments. The structural relationship among the 21 protons was arrived using ^{1}H NMR data. ^{1}H NMR spectrum of the ligand was recorded in DMSO-d6 medium using TMS as an internal standard and is shown in Figure-3. The shift values and the corresponding assignments are summarized in Table-4.

Table. 4: ^{1}H NMR spectral data and assignments of PMA.

S. No.	δ in ppm	Peak	Proton
1.	6.88	Singlet (1H)	Benzo ring
2.	6.92	Doublet (1H)	Benzo ring
3.	6.90	Doublet (1H)	Benzo ring
4.	7.96	Doublet (2H)	Acetophenone (o)
5.	7.65	Doublet (2H)	Acetophenone (m)
6.	7.66	Multiplet (1H)	Acetophenone (p)
7.	2.83	Doublet (2H)	CH_2 protons
8.	4.04	Triplet (1H)	CH proton
9.	2.77	Triplet (4H)	CH_2-N-CH_2
10.	3.26	Triplet (4H)	CH_2-O-CH_2
11.	6.01	Singlet (2H)	CH_2 protons

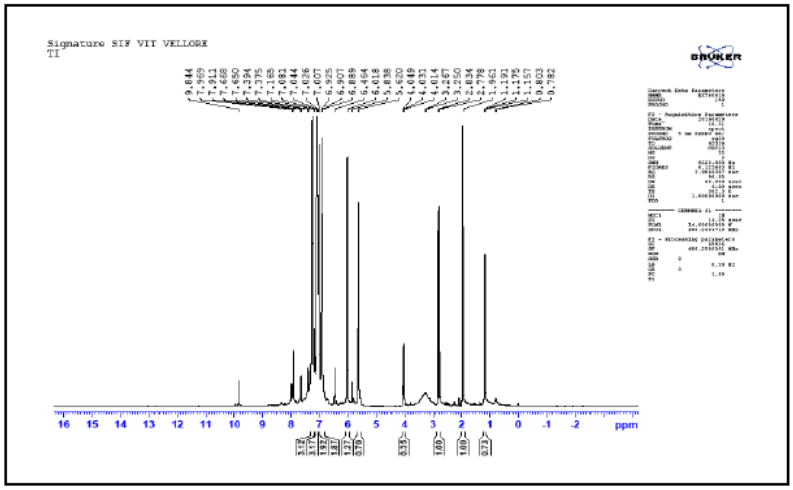


Figure-3 ^{1}H NMR spectrum of PMA.

3.5 ^{13}C NMR spectra

The results obtained from ^{13}C NMR helped to find out the number of carbons and their chemical environments. The structural relationship among the 20 carbons was elucidated using ^{13}C NMR data. ^{13}C NMR spectrum of the ligand was recorded in DMSO-d6 medium using TMS as an internal standard. The spectrum of the compound is shown in Figure-4. The shift values and the corresponding assignments are summarized in Table-5.

Table. 5: ^{13}C NMR spectral data and assignments of PMA.

S. No.	δ in ppm	No. of Carbons	Carbon
1.	141.62 – 151.57	2 C	Benzo ring
2.	111.25	1 C	O-CH_2-O
3.	118.38	2 C	Benzo ring
4.	129.91	1 C	Benzo ring
5.	121.67	1 C	Benzo ring
6.	136.73	1 C	Acetophenone
7.	128.54	4 C	Acetophenone
8.	134.76	1 C	Acetophenone
9.	192.26	1 C	Carbonyl carbon
10.	60.45	2 C	CH_2-O-CH_2
11.	40.49	2 C	CH_2-N-CH_2
12.	76.76	1 C	-CH- aliphatic
13.	77.08	1 C	CH_2

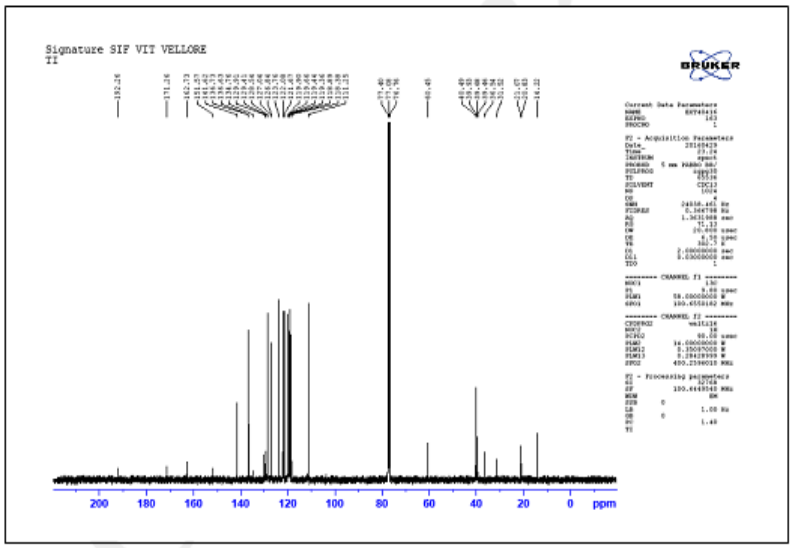


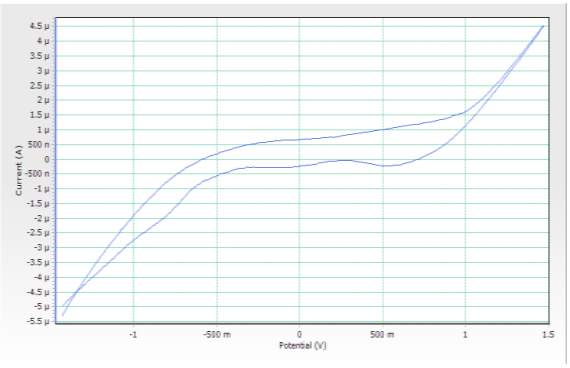
Figure. 4: ^{13}C NMR spectrum of PMA.

3.6 Cyclic Voltammetry

Cyclic voltammetry (CV) is an important electro analytical technique in many areas of chemistry. It is widely used to study a class of redox processes, for obtaining the stability of reaction products, the presence of intermediates in oxidation-reduction reactions, reaction and electron transfer kinetics and the reversibility of a reaction [17,18,19,20]. Cyclicvoltammetric behavior of complexes was recorded in the range from +1.5 to -1.5V in DMSO medium. The data obtained from cyclic voltammetry helped us to analyze the redox property of metals in the synthesized complexes. Complexes such as Mn-PMA, Co-PMA, Ni-PMA, Cu-PMA and Zn-PMA showed reduction process and also found to be irreversible in nature (Fig. 5a – 5e). The reduction and oxidation potentials are summarized in Table – 6.

Table. 6: Cyclic Voltammogram data of M-PMA complexes.

Compounds	E red1/2(V)	E ox1/2(V)	Ep(V)
Mn (II)-PMA	0.5940	-0.9888	-1.5828
Co (II)-PMA	0.7658	-1.2575	-2.0233
Ni (II)-PMA	0.2837	-1.4721	-1.7558
Cu (II)-PMA	0.7140	-0.7140	-1.4280
Zn (II)-PMA	0.4980	-0.7683	-1.2663



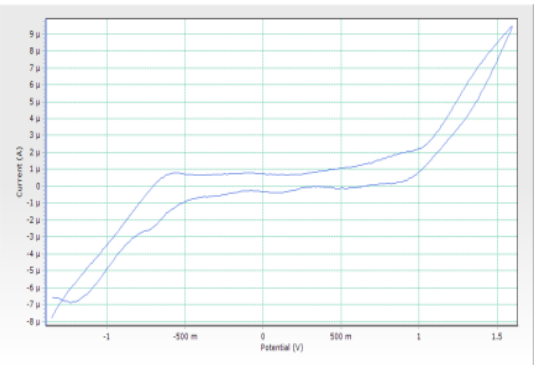
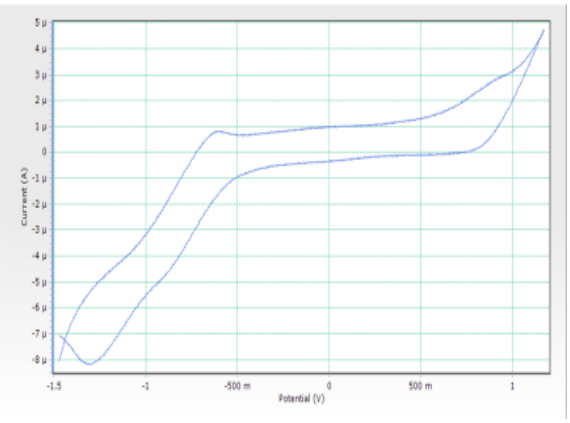


Figure-5a CV curve of Mn-PMA complex. Figure-5b CV curve of Co-PMA complex.



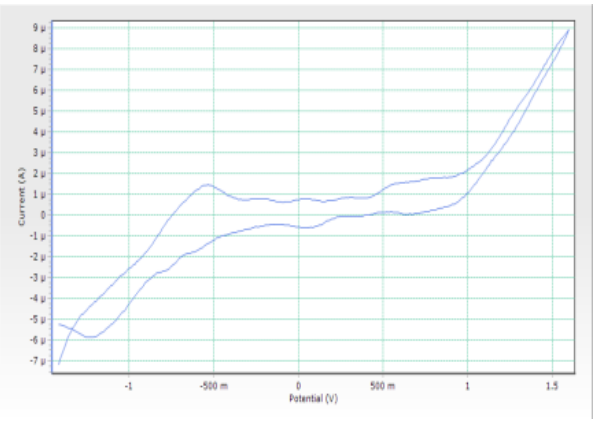


Figure- 6c CV curve of Ni-PMA. **Figure-7d CV curve of Cu-PMA.**

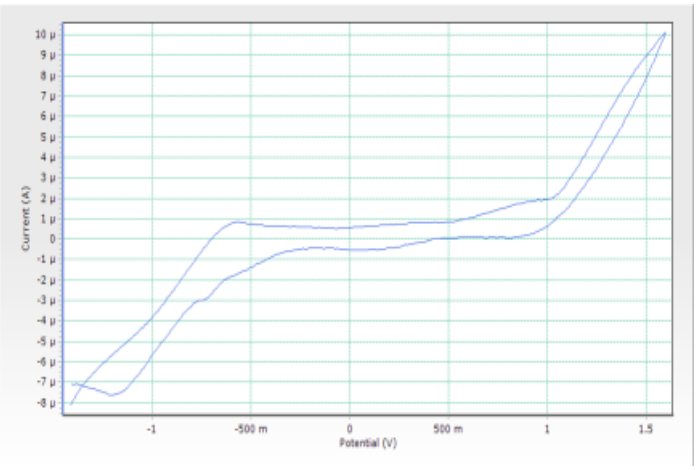


Figure-8e CV curve of Zn-PMA.

3.7 In vitro study - I

The prime focus on the synthesis of any antimicrobial compound is to inhibit the casual microbe without any side effect on the patients' metabolism. The antimicrobial activity of ligand and its metal complexes were done by in-vitro disc diffusion method in DMSO medium. The metal salts (MCl_2), ligand, metal complexes, the standard drug C*iprofloxacin*,

and the solvent DMSO were screened separately for their antibacterial activities at 100 µg/disc concentration, except the standard drug, which was tested at 10 µg/disc. The photographic plates of the tested microorganisms are shown in Figure 6a – 6d. The antibacterial activity was estimated on the basis of the size of inhibition zone formed on the seeded agar plates. Growth inhibition was compared with known antibiotics, viz., *Ciprofloxacin.* The Mannich base and its complexes exhibited varying degrees of inhibitory effects on the growth of the tested bacterial species.

As observed, the free ligand is moderately active against the bacterial species and it became more pronounced when it is coordinated to the metal ions. Referring to complexes, we note that the Ni (II) complex is more active as compared with other complexes. The order of antibacterial activity of the complexes is Ni>Cu>Mn>Co>Zn. Furthermore, the data show that *Staphylococcus aureus gram +ve* was inhibited to a greater degree by the Ni (II) complex.

A greater antibacterial activity of metal complexes is explained on the basis of Overtone's and Tweedy's concepts [21,22,23]. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors only the passage of lipid soluble materials, therefore lipo solubility is considered to be an important factor that controls the antibacterial activity. Tweedy's concept explains the increase of lipophilic character of the metal chelate. Upon chelation, the positive charge of the metal ion is partially shared with the donor atom present on the ligand and a π -electron delocalization over the whole chelate ring takes place. In this way, the lipophilic character of the metal chelate increases and favors its permeation through the lipoid layers of the bacterial membranes and blocks the metal binding sites in the enzymes of microorganisms[24]. This penetration disturbs the respiration process of the cell and thus blocks the synthesis of proteins, which restricts the further growth of the organisms[25].

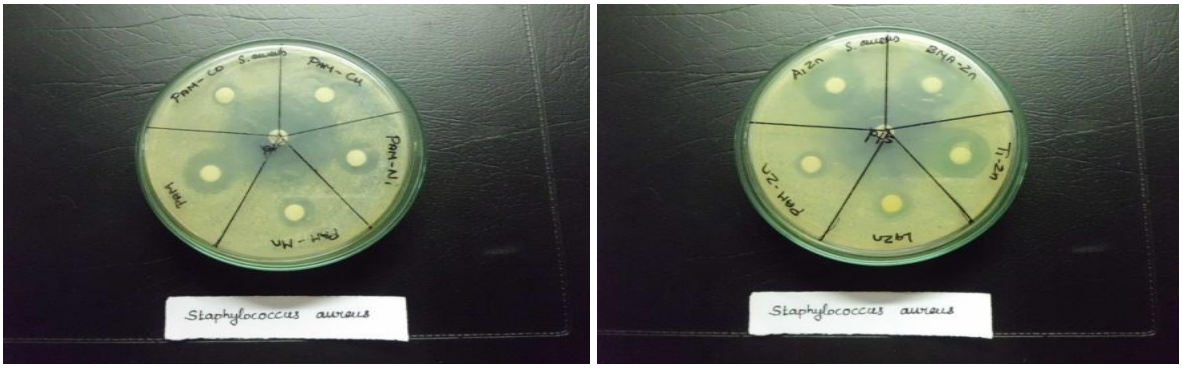


Figure-6a Antibacterial activities of PMA and its complexes on *Staphylococcus aureus.*

Figure-6b Antibacterial activities of PMA and its complexes on *Bacillus subtilis.*

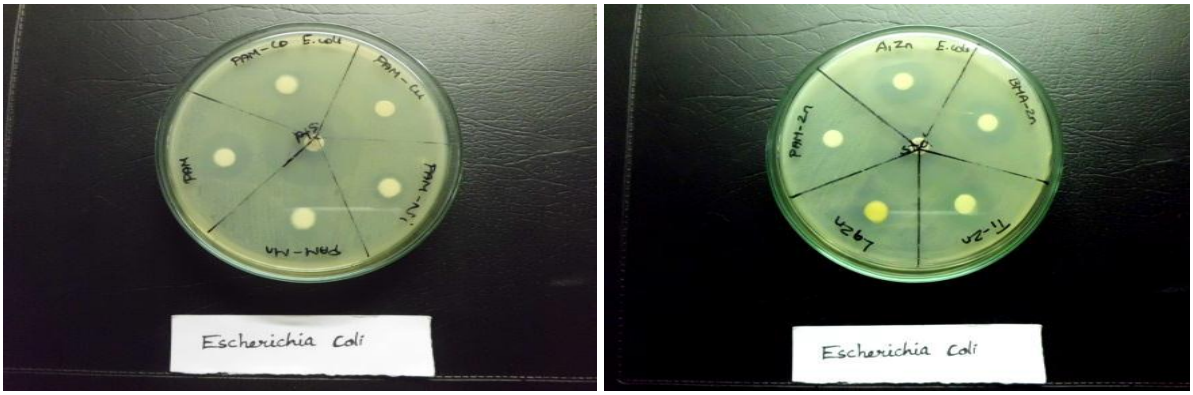


Figure-6c Antibacterial activities of PMA and its complexes on *Escherichia coli.*

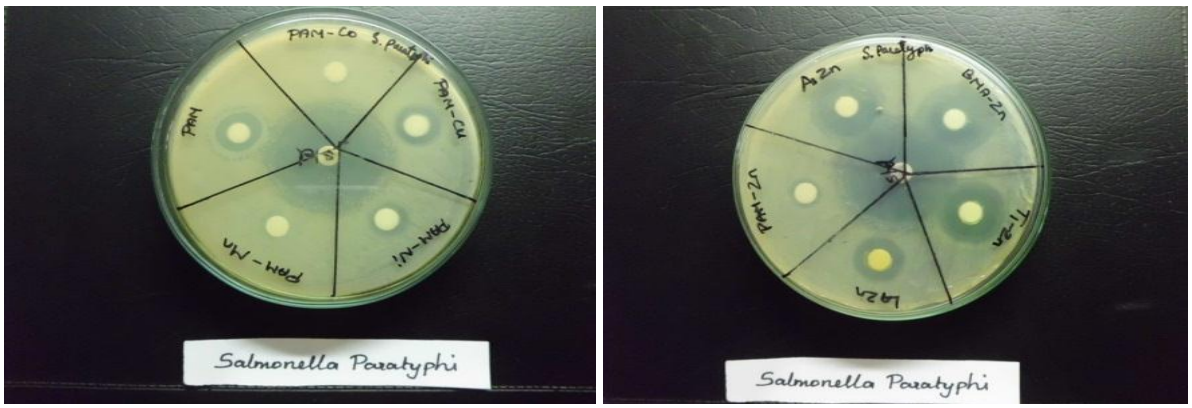


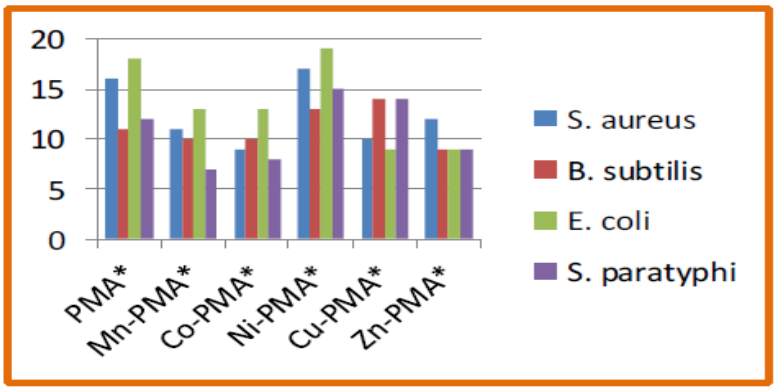
Figure-6d Antibacterial activities of PMA and its complexes on *Salmonella paratyphi.*

Table. 7: Antibacterial activity of PMA and its complexes.

Compounds	*Staphylococcus aureus gram (+ve)*	*Bacillus subtilis gram (+ve)*	*Escherichia coli gram (-ve)*	*Salmonella paratyphi gram (-ve)*
	Zone of Inhibition(mm)			
PMA*	16	11	18	12
Mn-PMA*	11	10	13	07
Co-PMA*	09	10	13	08
Ni-PMA*	17	13	19	15
Cu-PMA*	10	14	09	14
Zn-PMA*	12	09	09	09
Ciprofloxacin**	40	28	34	40

(*100 µ/disc and **10 µg/disc).

The Table-7 reveals that the inhibition by the ligand is relatively better than the complexes. Among the complexes, nickel complex has higher activity than the other complexes. Chelate ring of Ni enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and restricts further multiplicity of the microorganisms. The variation in the effectiveness of other complexes (Ni>Cu>Mn>Co>Zn) against different antibacterial organisms is not only depend on the nature of metal but also depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells. The chelating ring of Ni^{+2} reduces polarity and increases the lipophilicity of the bacterial membrane, interrupting normal cellular processes and enhancing the antibacterial activity of Ni^{2+} complex.



Graph-1 Comparative report on in vitro – I (antibacterial activity) of PMA and its complexes.

3.8 In vitro study - II

The antifungal activities of the ligand and its complexes were studied against *Candida albican* and *Aspergillus niger*. The metal salts (MCl_2), ligands, metal complexes, the standard

drug *Clotrimazole*, and the solvent DMSO were screened separately for their antifungal activities at concentrations of 100 µg/disc, except the standard drug, which was tested at 10 µg/disc. The photographic plates of tested microorganisms are shown in Figure 7a – 7b. Fungal species were more resistant to treatments with the new complexes. However, the synthesized complexes showed activity against these two fungi strains. The results on antifungal activity of the ligands show moderate activity while the complexes show higher activity against the fungi. The Cu-PMA complex shows higher activity when compared to other complexes and the order of activity against the fungi follow the order Cu>Ni>Co>Mn=Zn.

Due to the greater solubility, Cu (II) ions are adsorbed on the surface of the cell wall of microorganisms and disturb the respiration process of the cell and thus block the synthesis of the proteins that restricts further growth of the organisms. So, Cu (II) ions are essential for the growth-inhibitor effect. Such increased activity of the complexes can be explained on the basis of Overtone's concept and Tweedy's Chelation theory. On chelation, the polarity of Cu (II) ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the copper ion with donor groups. Further, it increases the delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity, enhances the penetration of the complexes into lipid membrane and restricts further multiplicity of the microorganisms.

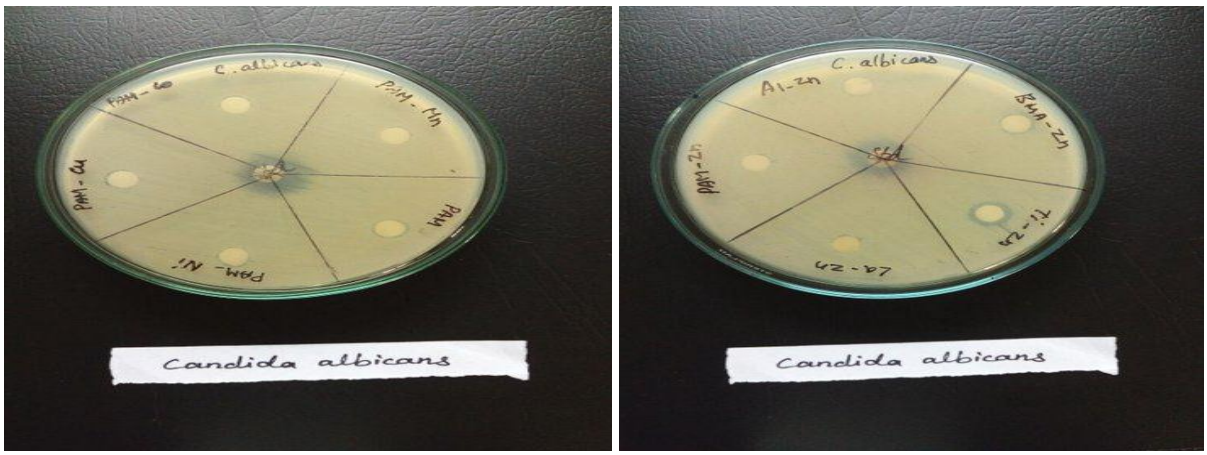


Figure. 7a: Antifungal activities of PMA and its complexes on *Candida albicans.*

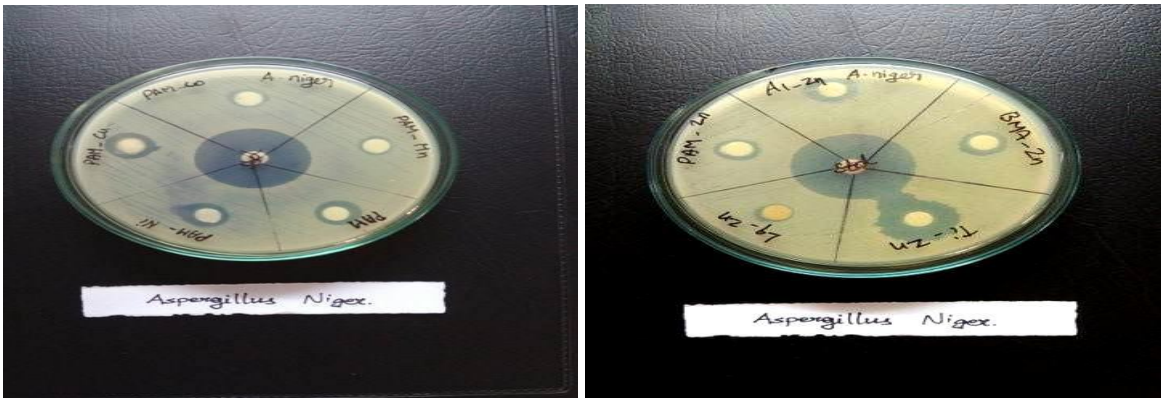
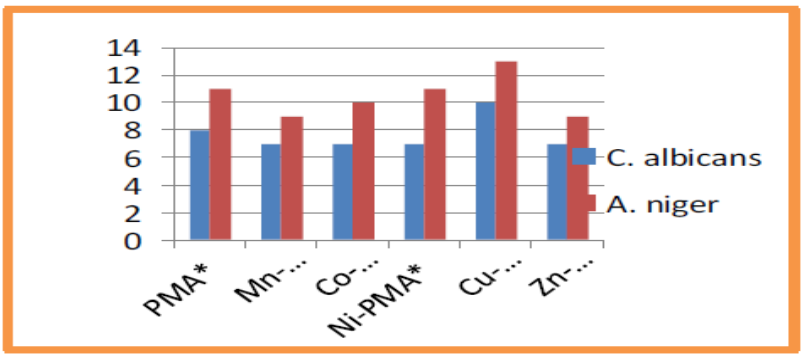


Figure. 7b: Antifungal activities of PMA and its complexes on *Aspergillus niger*.

Table. 8: Antifungal activity of PMA and its complexes.

Compounds	*Candida albicans*	*Aspergillus niger*
	Zone of Inhibition(mm)	
PMA*	08	11
Mn-PMA*	07	09
Co-PMA*	07	10
Ni-PMA*	07	11
Cu-PMA*	10	13
Zn-PMA*	07	09
Clotrimazole**	20	30

(*100 µg/disc and **10 µg/disc).



Graph. 2: Comparative report on in vitro – II (anti-fungal activity) of PMA and its complexes.

4. CONCLUSIONS

We have synthesized a Mannich base, 3-(Benzo[d][1,3]dioxol-5-yl)-3-morpholin-4-yl-1-phenylpropan-1-one, from the combinations of piperonal, morpholine and acetophenone. The structural elucidation was done using a range of analytical and spectral studies. The potentiality against microorganisms triggered us to screen the complexes for antimicrobial activities by in vitro methods. The complexes have shown greater tendency to prevent the

growth of microorganism than the ligand, individual metal ions and medium. The Ni-PMA complex has shown greater activity against bacteria than the other complexes. The moderate size of Ni^{2+}, relative to that of other metals, reduces polarity and increases the lipophilicity of the bacterial membrane, interrupting normal cellular processes and enhancing the antifungal activity of Ni^{2+} complex. The Cu-PMA complex has shown activity tremendously against fungies. The Cu (II) ions are adsorbed strongly on the surface of the cell wall of microorganisms and disturb the respiration process of the cell than the other metal ions, because of its higher solubility. The in vitro results suggested that all the synthesized metal complexes were effective and this finding is likely related to the better solubility, bioavailability and interaction with lipid membrane through intermolecular associations.[26,27] Increase in the lipophilicity of the complexes reduces the permeability barrier of the cells and slow down the normal cellular processes of the microorganisms, resulting in an increased antimicrobial activity**.** Thus it blocks the synthesis of the proteins that restricts further growth of the microorganisms.

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REFERENCES

1. Abdul Jameel. A, Syed Ali Padusha. M and Sulthan Syed Ibrahim. K, Asian J. Chem, 2011; 23: 1269.
2. Alhadi. A, Shaker. S.A, Yehye. W.A, Mohamed Ali. H and Abdullah. M A, Bull. Chem. Soc. Ethiopia, 2012; 26(1): 95.
3. Dong. Y, Narla. R K and Sudbeck E, J. Inorganic Biochemistry, 2002; 78: 321.
4. Popora. E and Berova. S, Bulgarius chemical abstract, 1981; 84: 184.
5. Shaelke. V A, Jadhav. S.M, Shankarwar. S.G, Munde. A.S and Chondhekar. T.K, Bull. Chem. Soc. Ethiopia, 2011; 25(3): 381.
6. Rahman. A U, Choudhary. M.I and Thomson. W.J, Bioassay Techniques for Drug Develepment, Harwood Academic Publishers, Netherlands, 2001.
7. Chandrasekaran. T, Suresh. M, Mashood Ahamed. F.M and Syed Ali Padusha. M, Pelagia Research Library, Der Chemica Sinica, 2014; 5(5): 81-90.
8. Alaghazh. M A, Bayoumi. H A, Ammar. Y A and Aldhlmani. S A, J. Molec Struct, 2013; 1035: 383.
9. Rekha. S and Nagasundara. K R, Ind. J. Chem, 2006; 45: 2421.

10. Sathya D, Senthil Kumaran J and Jayachandramani N, Research journal of pharmaceutical, biological and chemical sciences, 2012; 3(2): 905.
11. Anbu. S, Kandaswamy. K, Sathya Moorthy. P, Balsubramanian. M and Ponnuswamy. M.N, Polyhedran, 2009; 28: 49.
12. Raman N, Esthar S, Thangaraja C, J. Chem. Sci., 2004; 116(4): 209-213.
13. Lukose. G, Mohanan. K, Saju. S and Rahim. S, J. Che. and Pharm. Research, 2013; 5(5): 241.
14. Sabastiyan. A and Yosuva Suvaikin. M, Pelagia Research Library, Advances in Applied Science Research, 2012; 3(1): 45.
15. S. Murugesan, S. Sathiyamoorthy, J. Pharm. Res., 2011; 4: 2679.
16. Kriza. A, Viorica Ababei. L and Stanica. N, J. Serb. Chem. Soc, 2010; 75(2): 229.
17. Hwang. T.L and Shaka. A.J, J. Mag. Res. Series A, 1995, 112, 275. Origin, 7.5 Ed., Origin Lab Corporation, 2006.
18. Tribolet. R and Sigel. H, Eur. J. Biochem, 1987; 163: 353.
19. Sathya. D, Senthil Kumaran. J and Jayachandramani. N, Research journal of pharmaceutical, biological and chemical sciences, 2012; 3(2): 905.
20. Emmanuel. J. et al IOSR Journal of Applied Chemistry (IOSR-JAC) e-ISSN: 2278-5736, Sep. - Oct. 2013; 5(3): 50-55.
21. Ajaykumar. D et al, Int. J. Electrochem. Sci., 2009; 4: 717-729.
22. Radha. S, Mothilal. K. K, Thamaraichelvan. A and Elangovan, Journal of Chemical and Pharmaceutical Research, 2016; 8(8): 202-211.
23. Ahmed. A. et al Bioinorganic Chemistry and Applications, 2012, Article ID 795812.
24. Misbah Ur Rehman, Muhammad Arif, Muhammad Imran, Muhammad Farooq, American Journal of Chemistry, 2014; 4(1): 10-21.
25. Rajavel. R, Senthilvadivu. M and Anitha. C, E-Journal of Chemistry, ISSN: 0973-4945, 2008; 5(3): 620-626.
26. Wang. P, Zhang. Z, Zhang. H, Fan. Z, Transition Met. Chem., 2008; 33: 835.
27. Patel, P. K, Patel. P. D, Int. J. ChemTech Res., 2010; 2: 1147.
28. Kannan. S and Syed Ali Padusha. M, Int. J. of ChemTech Research, 2017; 10(6): 770-783.
29. Kannan. S and Syed Ali Padusha. M, World J. of Pharmaceutical Research, 2017; 6(10): 1138-1152.