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Synthesis, Characterization, Larvicidal Activity and Antimicrobial Activity of Transition Metal Complexes of Pyrrole-2-Carboxaldehyde with Cysteine

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ABSTRACT

The Schiff base ligand was prepared by condensation of pyrrole-2-carboxaldehyde with cysteine. Cu(II), Co(II), Mn(II), Zn(II) and Ni(II) complexes of above ligand was synthesised as well. The synthesised ligand and complexes have characterized by Powder XRD, SEM and EDAX. The antimicrobial activity of the synthesized ligand and its complexes have been tested for their antibacterial activity against bacterial species Basillus subtilis, Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, Pseudomonaos aeruginosa, Staphylococcus aureus and fungal species Candida albicans and Aspergillus niger. The result found that the metal complexes were more active than the ligand. Antioxidant activities of metal complexes have also been studied. The larvicidal activity of copper complex showed increased mortality rate than the ligand.

Keywords:- Pyrrole-2- carboxaldehyde, Cysteine, Transition metal complex, Antimicrobial activity.

I. INTRODUCTION

The Schiff bases have pronounced biological activities [1],[2] and form a class of important compounds in medicine and pharmaceutical field. The chelating ability of analytical and biocidal application of Schiff bases have attracted remarkable attention[3]-[8]. In continuation of these series of investigation[9]-[18], attempts have been made to synthesize the new Schiff base complexes. Transition metal complexes are of great significance on account of their unique coordination and structural properties and their utilities as bio-inorganic models[19]-[23]. In recent years, extensive research in chemistry of metal chelates involving chelating Schiff base containing nitrogen, oxygen and sulphur donor sites have steadily grown in many areas including synthesis, structure elucidation, reaction kinetics, redox behaviour and biological reactions.

In this paper the metal complexes of Cu(II), Co(II), Mn(II), Zn(II) and Ni(II) with the Schiff base derived from pyrrole-2-carboxaldehyde with cysteine have been synthesized. The ligand and the metal complexes have been characterized by powder XRD and SEM. The ligand and their metal complexes have been sereened for their antimicrobial activities using the well diffusion method against the selected bacteria and fungai.

II. EXPERIMENTAL

2.1 Materials

All the chemicals and solvents used in the present work were of analytical grade. Pyrrole-2- carboxaldehyde, L-Cysteine were purchased from sigma aldrich. Cu(II), Co(II), Mn(II), Zn(II) and Ni(II) chlorides and the solvents were purchased from Merck.

2.2 synthesis of Schiff base ligand Potassium(E) -2-(((1HPyrrol-2-yl) methylene) amino) 3-mercapto propanate (P1)

Pyrrole-2-carboxaldehyde (0.01 mol) is dissolved in 20 ml MeOH and added 20 ml methonic solution of L-Cysteine (0.01 mol) containing KOH (0.01 mol). The solution obtained was heated at 60℃ for 9 hours. Brownish yellow solution was formed. The volume of the solution is reduced to half. Filtered the precipitate, washed with ether followed by ethanol and dried in desiccator.

2.3 Synthesis of Schiff base metal complexes

To the hot methanolic solution of Schiff base ligand (0.01 mol), and the methanolic solution of metal ions ($CoCl_2.6H_2O$, $CuCl_2$. $2H_2O$, $NiCl_2$. $2H_2O$, $MnCl_2$. $2H_2O$, $ZnCl_2$) was added drop by drop at 60℃ in 1:2 (metal:ligand) molar ratio. The mixture was then refluxed for 1 hour the intensity of the colour becomes translucent. The resulting mixture was filtered out, washed repeatedly with ether and dried in desiccator.

2.4 Antimicrobial activity:

2.4.1. Test organisms:

Bacterial species Bacillus subtilis, Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, Pseudomonos aeruginosa, Staphylococcus aureus and fungal species Candida albicans and Aspergillus niger were used as test organisms.

The Schiff base ligand and its metal complexes were screened against bacterial species such as Bacillus subtilis, Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, Pseudomonos aeruginosa , Staphylococcus aureus and fungal species like Candida albicans and Aspergillus niger in agar well diffusion method. The Solvent used for dissolving the synthesised compounds was DMSO.

2.4.2.Experimental methods:

Muller hinton agar medium (20ml) was poured into each petri plate, and plates were swabbed with 100 µl inoculated of the test microorganisms and kept for 15 minutes for adsorption . Using sterile cork borer of 8mm diameter, wells were bored into the seeded agar plates, and these were located with a 100µl solution of each compound in DMSO. All the plates were incubated 37°C for 24 hrs .After incubation , the inhibition growth was analysed and the results were recorded.

2.5 Antioxidant assay (Free radical scavenging activity).

The free radical scavenging activity of the Schiff base ligand P1 and its Cu(II), Co(II), Mn(II) Zn(II) and Ni(II) test samples were determined using 2,2-diphenyl-1-picrylhydrazyl (DPPH) method[12].The different concentrations of test compound (20, 40, 80 µg) and standard vitamin-C were taken in different test tubes, and volume of each test tube was adjusted to 100 µl by adding DMSO. To the sample solutions in DMSO. Methanolic solution of DPPH was added to these tubes. The tubes were allowed to stand for 15 minutes. The control experiment was carried out the same but without the any test samples. The absorbance was measured at 515 nm. Radical scavenging activity was calculated by the following formula.

% Radical scavenging activity

$$= \left[\frac{\text{Absorbance of control OD - Absorbance of sample OD}}{\text{Absorbance of control OD}} \right] \text{x } 100$$

III. RESULTS AND DISCUSSION

The condensation of Pyrrole-2-carboxaldehyde with cysteine give the schiffbase ligand Potassium (E)-2-(((1HPyrrol-2-yl) methylene) amino) 3-mercapto propanate (P1). The ligand was coordinated with Cu^{2+}, Co^{2+}, Mn^{2+}, Zn^{2+} and Ni^{2+} ions separately to give colored complexes respectively M2(Cu), M3(Co), M4(Mn), M5(Zn) and M6(Ni). All the metal complexes were found to be stable at room temperature and insoluble in common solvents such as EtOH, MeOH but soluble in DMSO and DMF.

3.1 XRD

The powder XRD patterns of ligand P1 and Cu(II) complexes are recorded in the range 2θ = 0-80 Å were shown in Fig 1. The diffraction pattern revals the crystalline nature of the copper complex. The crystalline size of the copper complex was calculated from Scherre's formula [24].

$$d_{XRD} = 0.9\lambda/\beta \cos\theta$$

Where λ is the wavelength, β is the full-width half maximum of the characteristic peak and θ is the diffraction angle for the h k l plane. From the observed XRD patterns, the average crystalline size for the ligand P1 and Cu(II) complex P2(Cu) are found to be 27.24 nm and 26.72 nm respectively. This suggests that the ligand and the complex are in a nanocrystalline phase.

3.2 SEM and EDAX studies

The morphology of the ligand and the metal complex have been illustrated by the Scanning Electron Microscope (SEM). The SEM images of ligand P1 and Cu(II) complex were shown in Fig 2. SEM picture of the metal complexes show that the particles are agglomerated with controlled morphological structure and the presence of small grains in non-uniform size . The SEM image of Ligand exhibit flower like morphology whereas Cu(II) complex exhibit needle shaped species. The average grain size (~ 42.69,76.45 nm) respectively. The EDAX images of ligand P1 and Cu(II) complex were shown in Fig.3. The results by Energy Dispersive X-ray Analysis (EDAX) data indicated that ligand P1 obtained C, N, O, K and S peaks. Cu(II) complex exhibit C, O, S, K, Cu, and Cl peaks, which shows presence of copper oxides.

3.3 Antioxidant activity

The synthesized Schiff base and it's metal complexes were screened for free radical Scavenging activity by the DPPH method[25]. The results of the free radical scavenging activity of the ligand and it complexes at different concentrations are shown in Fig 4. Ni(II) complex have exhibited a good free radical scavenging activity. Whereas Mn(II), Zn(II), Cu(II) complexes have shown moderate activity. Ligand M1 and Co(II) showed less activity. The metal complexes were exhibited higher scavenging activity than the Schiff base ligand. The synthesized compounds scavenged the DPPH radical in a concentration dependent manner.

3.4 Antimicrobial activity

The antibacterial and antifungal activity results of the Schiff base ligand and their Cu(II),Co(II), Mn(II), Zn(II) and Ni(II) complexes were given in table 1.The presence of clear zones noted that the compounds were active. The zone of inhibition was measured in millimetres. The antimicrobial activities of ligands and its metal complexes are shown in Fig 5-6.

The Schiff base ligand and its metal complexes were screened against bacterial species Bacillus subtilis, Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, Pseudomonos aeruginosa , and Staphylococcus aureus and fungal species Candida albicans and Aspergillus niger. P2(Cu) complex showed good activity against all the bacterial species .The P2(Cu) complex showed 13mm zone of inhibition against Escherichia coli. These values are greater than the control Amikacin. P3(Co)complex showed high activity against Klebsiella pneumoniae and moderate activity against Bacillus subtilis, Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus. P4(Mn) complex showed high activity against Pseudomonos aeruginosa and moderate activity against Bacillus subtilis ,Bacillus cereus, Klebsiella pneumoniae, Escherichia coli and Staphylococcus aureus. P5(Zn) complexe showed high activity against Pseudomonas aeruginosa and moderate activity against other bacterial species and no activity against Staphylococcus aureus and Bacillus cereus .P6(Ni) complex showed high activity against Pseudomonas aeruginosa and moderate activity against Bacillus subtilis ,Bacillus cereus , Staphylococcus aureus and Klebsiella pneumoniae but no activity against the Escherichia coli. It is found that metal complexes have higher antibacterial activity than the schiffbase ligand[26]. Such increased activity of the metal complexes can be explained on the basis of overtone's concept and chelation theory[27],[28]. On chelation the polarity of the metal ion will be reduced due to the overlapping of the ligand orbital and partial sharing of positive charge of the metal with donor groups[29]. It increases the delocalization of π-electrons over the whole chelate ring and enchances the lipoplicity of the complexes. This increased lipoplicity enchances the penetration of the complexes into lipid membranes and block the metal binding sites in the enzymes of microorganisms.

P2(Cu), P3(Co) and P6(Ni) complexes showed moderate antifungal activity against the Candida albicans and Aspergillus niger. P4(Mn), P5(Zn) complexes have no antifungal activity. Antifungal activity of these complexes is obtained to be increased as the stability of the complex increased . But ligand P1 exhibits moderate antifungal activity for all the species screened. From the result, it was concluded that P2(Cu) complex showed higher antimicrobial activity than other metal complexes. P5(Zn) complex showed lower antibacterial activity and P4(Mn) and P5(Zn) complex showed lower antifungal activity. P2(Cu) compound can be tested for invivo studies and can further used as drugs for Escherichia coli . The antimicrobial activity depends on the molecular structure of the compound, the solvent used [30] and the species screened under consideration[31].

3.5 Larvicidal activity

The larvicidal activity of the schiffbase ligand and the copper complex was performed against the larvae of culex and the result of mortality values are listed in table 2,3. The pictorial representation of larvicidal activity is shown figure 7.

LC50 value of copper complex = 30PPm

LC90 value of copper complex = 50PPm.

LC50 : Lethal concentration that kills 50 % of the exposed larvae

LC90 : Lethal concentration that kills 90 % of the exposed larvae

The metal complex showed enhanced larvicidal activity than the schiffbase. The increased mortality rate observed for cu complex can be attriubuted to the increase in lippophilicity on complexation [32]. Chelation increases the lipophilice nature of the central metalatom, which in turn, favours the molecules in crossing the cell membrane of the microorganism and enhancing larvicidal activity of complex.

TABLE 1:

ANTIMICROBIAL ACTIVITY OF P1 AND THEIR METAL COMPLEXES

ngal activit	A.niger	-	13	6	-	-	-		13

Ligand / Complexes	Antibacterial activity						
	B. subtil	B. cereus	E. coli	K.pneumoniae	P.aeruginosa	S. aureus	C.albicans
P1	6	11	6	7	5	6	9
P2 (Cu)	13	22	13	24	23	15	-
P3 (Co)	6	4	6	8	7	5	-
P4 (Mn)	5	5	5	6	11	5	-
P5 (Zn)	5	-	5	5	8	-	-
P6 (Ni)	5	6	-	6	8	5	5
Amikacin	30	33	12	34	31	18	
Nystatin							18

Table 2

Larvicidal activity of ligand and their Coper(II)complex

Compound	Concentration ppm	Mortality rate of different time intervals		
		24	48	72
P1	1000	45	50	50
P2	1000	80	80	80

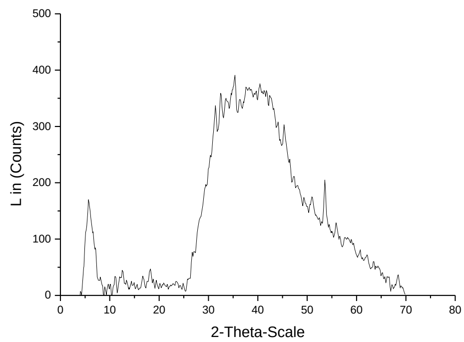
Table 3:

Larvicidal activity of ligand and their Coper(II)complex

Compound	Concentration ppm	Mortality rate of different time intervals					
		12	24	36	48	60	72
	20	20	40	45	45	45	45
	40	60	85	10	10	10	10

P2				0	0	0	0
	60	65	90	10 0	10 0	10 0	10 0
	80	75	10 0	10 0	10 0	10 0	10 0
	100	85	10 0	10 0	10 0	10 0	10 0

P1



P2(Cu)

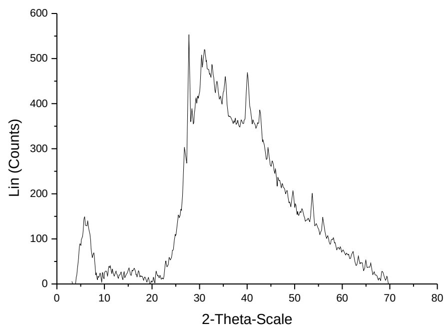
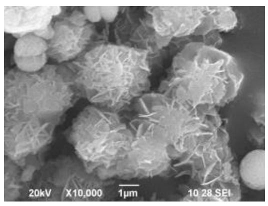
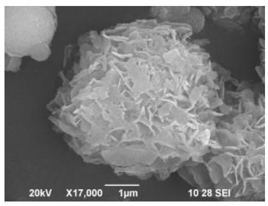


Fig 1 : Powder XRD pattern of ligand P1 and P2(Cu) Complex





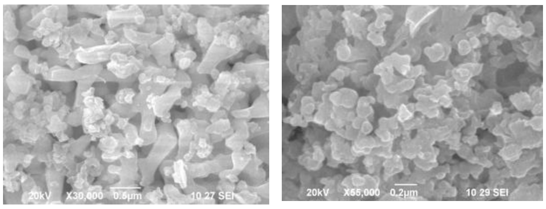
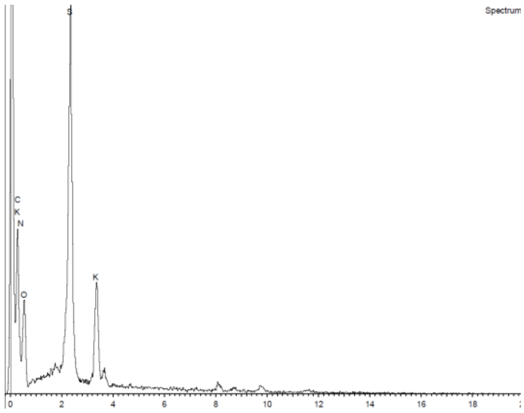


Fig 2 : SEM images of P1 and its metal complex

P1



P2(Cu)

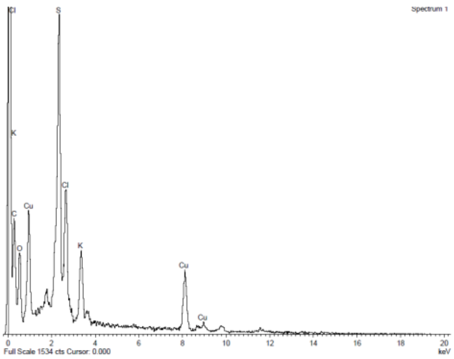


Fig 3 : EDAX spectrum of P1 and their metal complex

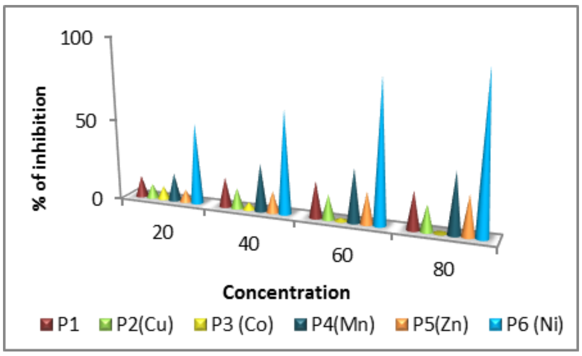


Fig 4 : Antioxidant activity of P1 and their metal complexes

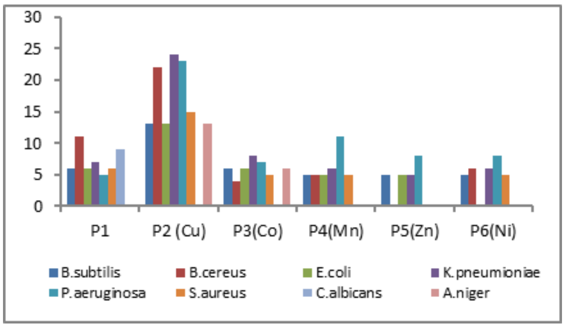


Fig 5 : Antimicrobial activities of P1 and their metal complexes

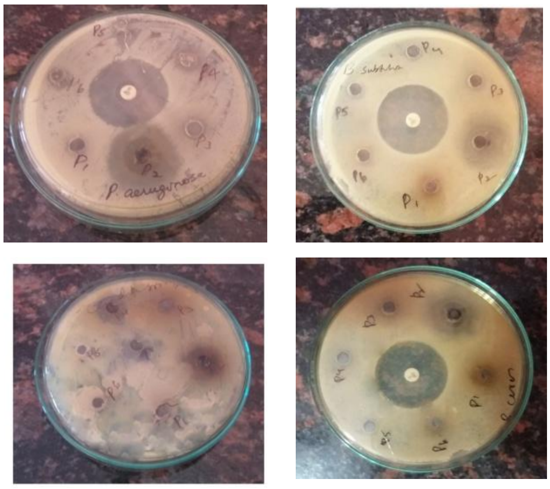


Fig.6 : Inhibition zone against screened bacteria and fungi by the ligand and complexes

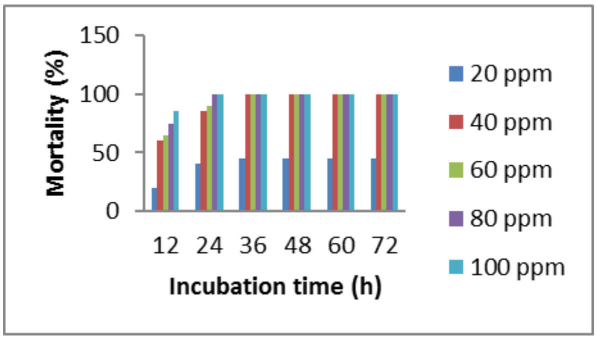


Fig 7 : Larvicidal activity of copper to complex

IV. CONCLUSION

The Schiff base ligands and it's P2(Cu), P3(Co), P4(Mn), P5(Zn) and P6(Ni) complexes were synthesized. The synthesized complexes were characterised by XRD, SEM. They were tested for Antioxidant activity. The XRD, SEM and EDAX analysis explains the crystalline and morphological structure of the ligand and complexes. EDAX studies gave information about metal and elemental composition. The Antioxidant activities indicate that the complexes show higher activity than the ligand. The antimicrobial studies showed that the Schiff base ligand possesses mild activity and metal (II) complexes possesses higher activities against different bacterial and fungal strains. From the results it was concluded that copper complex P2(Cu) exhibits higher antimicrobial activity than ligand and other metal complexes. P2 (Cu) compound can be used as drugs after invivo studies. The larvicidal activity of copper complex showed increased mortality rate than the ligand.

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