# Synthesis Characterisation and Application of Copper Complexes with N-(4-pyridyl) isonicotinamide.

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***Abstract :*** Two complexes of copper with N-(4-pyridyl-) Isonicotinamide was prepared by solvent based synthesis method. Their structure were identified by various spectrioscopic method. Their antimicrobial and catalytic activities are verified.

***Key word*** **- Isonicotinamide, Antimicrobial properties, MIC analysis, Photocatalyst.**

## I. INTRODUCTION

Nicotinic acid and its derivatives are excelent biological chelating ligands which posses N, S, and O donor atoms that can coordinate with metal atoms to form coordination complexes. Metal complexes of these ligands show many important biological activities such as antibacterial, antifungal, antiviral, antitumor, anti-inflammatory etc. and are also found to be pharmacologically and physiologically active. Many such metal complexes of nicotinic acid and its derivatives have supramolecular association i.e. 3D framework structure via hydrogen or covalent bonds. Pyridine derivatives possess a diverse array of bioactivities as well as playing crucial roles for physiological functions[1-4]. They have been extensively used as ligands in the formation of coordination compounds as medicinal agent[5]. Isonicotinamide is a versatile reagent in crystal engineering for the synthesis of binary crystals with hydrogen bond donor groups (carboxylic acid, phenol)[6]and coordination compounds with silver salts ($AgBF_4$, $AgPF_6$, $AgO_3$-$SCF_3$)[7]. In the present work we prepare two binuclear complexes of copper. Application of the complexes were also studied.

## II. EXPERIMENTAL

### A. Synthesis of N-(4-Pyridyl)Isonicotinamide

1.4028g/6.8mmol DCC (NN'-Dicyclohexyl Carbodiimide) and 0.8248g/6.7mmol 4-Pyridine carboxylic acid are added to 30ml of ethyl acetate and stirred for 30minutes. The mixture was added gradually to cold solution of 0.6306g/6.7mmol 4-Aminopyridine in 30ml of ethyl acetate and stirred for 24hours at room temperature. Resultant solution was filtered and kept in cold condition. White crystals of N-(4-Pyridyl)Isonicotinamide abbreviated as **4-pina** was started to separate within three days. Crystals are purified by washing with methanol.

### B. Synthesis of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$

0.1000gm/0.5mmol of 4-pina was dissolved in 10ml of methanol. 0.3164ml/4mmol of pyridine was dissolved in it. 0.370gm/1mmol $CuClO_4$ was dissolved in minimum amount of methanol. Ligand solution was added slowly to $CuClO_4$ solution which is kept undisturbed. Dark blue crystals were formed slowly.

### C. Synthesis of $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$

0.1000gm/0.5mmol 4-pina was dissolved in 10ml of methanol. 0.3124gm/2mmol bipyridine was dissolved in it. 0.370gm/1mmol $CuClO_4$ was dissolved in minimum amount of methanol. Ligand solution was added slowly to $CuClO_4$ solution which is kept undisturbed. Light blue crystals were formed slowly.

Characterisation of the complexes was done by various spectroscopic analysis. Its antimicrobial and catalytic properties are studied.

## III. RESULTS AND DISCUSSION

### A. General properties

General properties include Physical and analytical data, molar conductivity value, and the solubility. The color and other physical properties are listed in table 1, the elemental analysis results are given in table. 2 and molar conductivity value were given in table 3. Elemental analysis and molar conductivity value indicates the stochiometry of the complexes. The complexes are highly soluble in DMSO and DMF and slightly soluble in methanol.

Table.1. Physical and analytical data of the ligand and complexes

| Ligand/ Complex | Color | Mol.Wt | M.P(°C) | Yield (%) |
|---|---|---|---|---|
| Ligand – 4-pina | White crystals | 199 | $280^0$C | 20 |
| $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ | yellow | 1498.88 | $220^0$C | 65.30 |
| $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ | yellow | 1491.892 | $250^0$C | 68.26 |

Table.2.Elemental analysis data of ligand and complexes of 4-pina

| Ligand/ Complex | Found/calculated % | | | | |
|---|---|---|---|---|---|
| | C | H | N | S | Metal |
| (4-pina) | 69.98 (66.33) | 12.20 (4.5) | 12.55 (21.10) | - | - |
| $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ | 37.43 (40.83) | 3.27 (4.34) | 9.36 (10.27) | | 9.95 (8.47) |
| $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ | 41.50 (41.05) | 6.32 (3.82) | 10.42 (10.33) | | 9.3 (8.52) |

CHN analysis carried out from SAIF STIC Cochin and % of metal was calculated gravimetrically. They match closely with the calculated values,

Table. 3. Molar Conductance value of the complexes of 4-pina

| Complex | Molar Conductance |
|---|---|
| $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ | 36.7 |
| $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ | 28.7 |

From the molar conductance value it was clear that all these complexes are nonelectrolyte[8]

**B . Characterisation of the ligand**

Ligand N-(4-Pyridyl)Isonicotinamide (4-pina) was characterised by $^1H$ NMR spectra. The spectra of the synthesized ligand was recorded in $CDCl_3$ solvent, at the National Institute for Interdisciplinary Science and Technology, Thiruvananthapuram. The multiplets within the range $\delta$ = 8.73, 7.94 and 7.26ppm correspond to hydrogen of aromatic ring

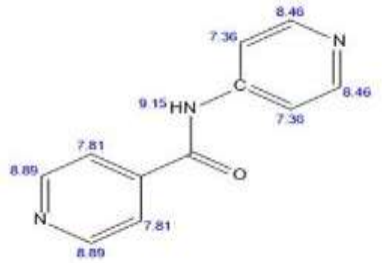


Fig.1. Str. of 4-pina

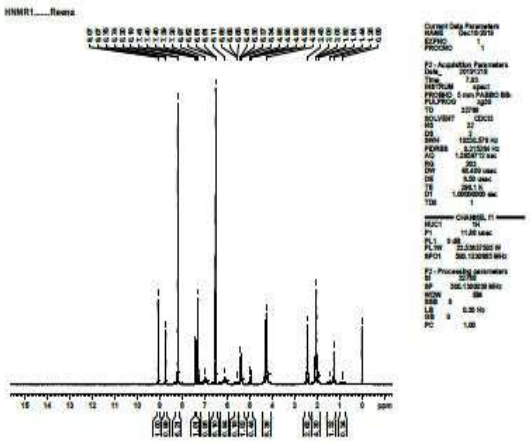

Fig.2. $^1H$ NMR spectra of 4-pina

**C. Characterisation of the complexes**

Characterisation of the complexes of 4-pina was done through various spectral studies.

**i) Infrared Spectroscopy**

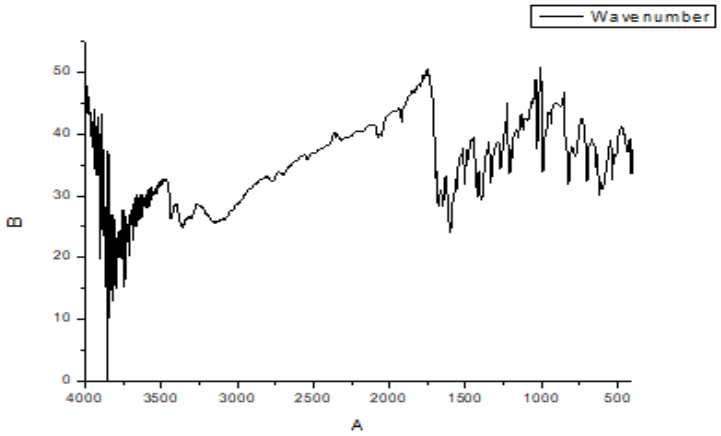


Fig.3. Infrared spectra of 4-pina

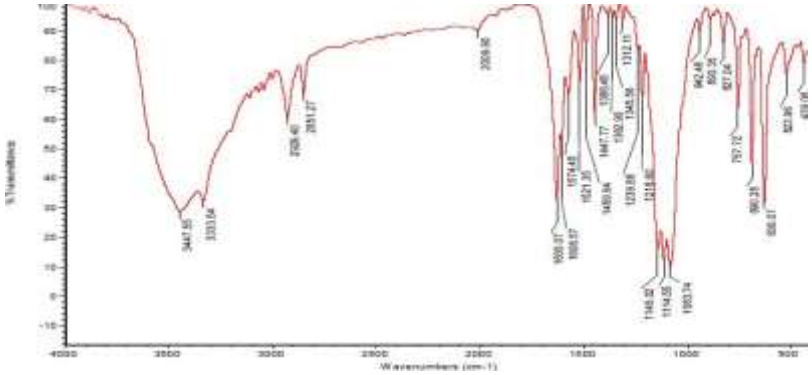

Fig.4. Infrared spectra of [$Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2$] 4Py $6H_2O$

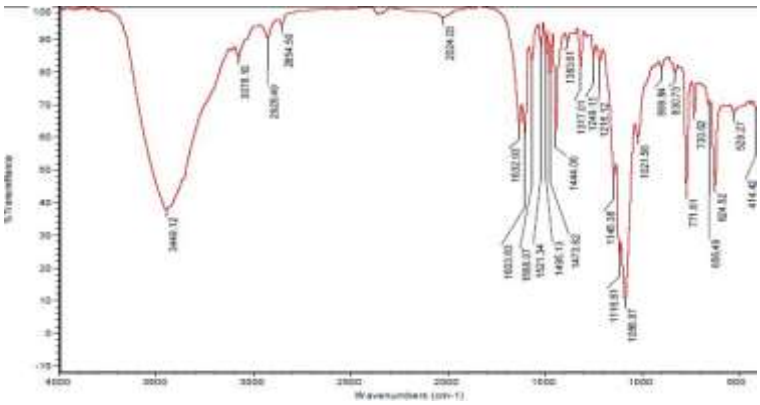

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Fig.5.Infrared spectra of [$Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2$] 2Bpy $6H_2O$

Table.4. Infrared spectral bands ($cm^{-1}$) of the complexes of 4-pina

| Complex | υN-H | υC-H | υC=O | υ C=N | υ C-N |
|---|---|---|---|---|---|
| [$Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2$] 4Py $6H_2O$ | 3447 | 2929 | 1630 | 1608 | 1574 |
| [$Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2$] 2Bpy $6H_2O$ | 3440 | 3075 | 1632 | 1603 | 1521 |

IR spectra of of 4-pina and its complexes were given in fig.3 to fig.5 and the main absorption bands are given in table.4. Absorption band from 3417 & 3440$cm^{-1}$ is due to stretching vibration of N-H bond; absorption band from 2929 & 3075 $cm^{-1}$ is due to C-H bond; absorption from 1630 & 1632 $cm^{-1}$ is due to stretching vibration of C=Obond; absorption band from 1608 &1521603$cm^{-1}$ is due to C=N bond and that from 1574 &1521$cm^{-1}$ indicate C-N bond.

**ii) Electronic Spectroscopy**

UV Spectrum of 4-pina

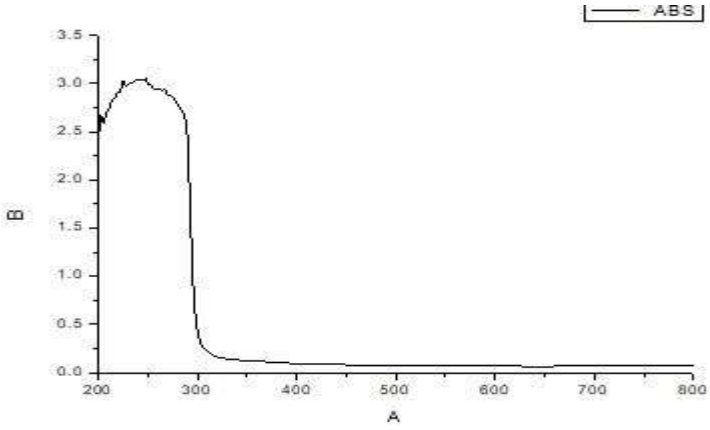


Fig.6. UV Spectrum of 4-pina

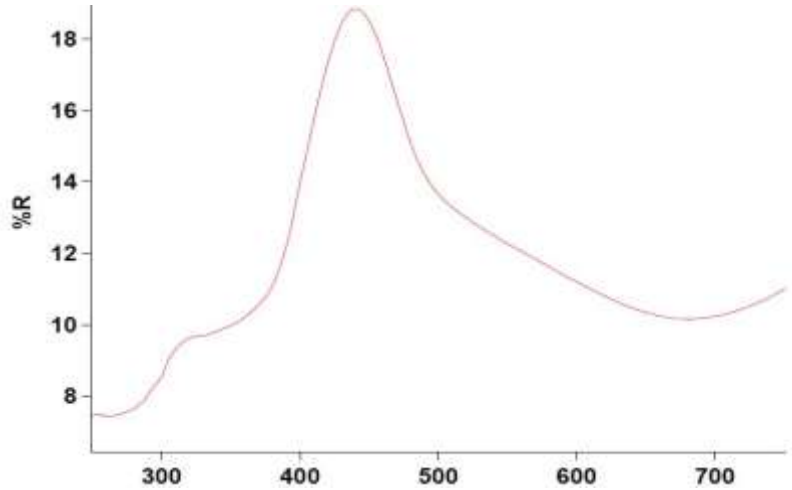


Fig.7. Solid state UV Spectrum of [$Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2$] 4Py $6H_2O$

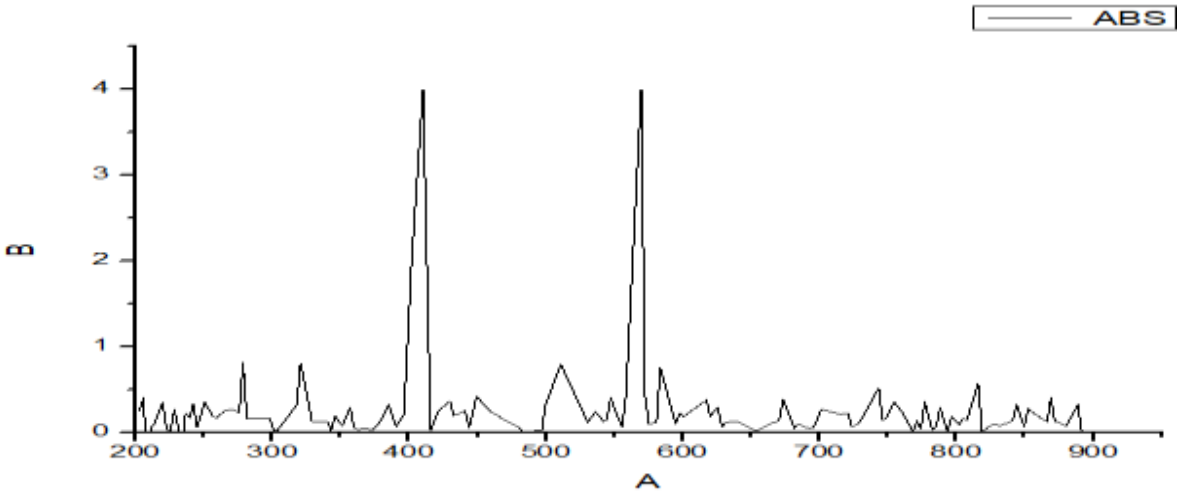


Fig.8. Solid state UV Spectrum of [$Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2$] 2Bpy $6H_2O$

Table.5. Electronic spectral bands of complexes.

| Complexes | Bands (nm) | Assignment | Geometry |
|---|---|---|---|
| 4-pina | 250 | $\pi \rightarrow \pi^*$ | |
| [$Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2$] 4Py $6H_2O$ | 330<br>440 | $n \rightarrow \pi^*$<br>LMCT | Octahedral |
| [$Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2$] 2Bpy $6H_2O$ | 400<br>575 | LMCT<br>d-d | Octahedral |

UV spectrum of the ligand and its complexes are given in fig. 6 to fig.8 and the spectral bands are given in table.5.

**iii) Mass spectroscopy**

Mass spectrum of $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$

The molecular ion peak of $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ is observed at 1497.25amu (calc. 1491.892). The base peak is observed at 950amu (100) (calc.953.46) $[Cu_2C_{31}H_{27}N_7O_{14}Cl_3]^+$. A medium peak at 1053.44amu (58.57) is due to the formation of $[Cu_2C_{31}H_{27}N_7O_{18}Cl_4]^+$. The mass spectrum of $Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ is given in fig.

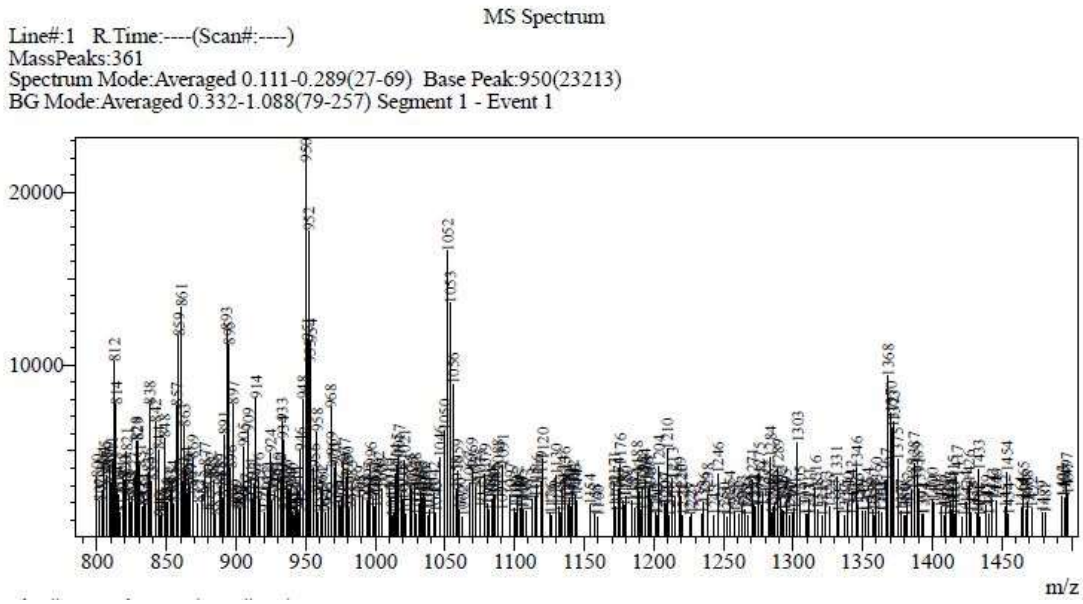


Fig.9. Mass spectrum of $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$

Mass spectrum of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$

The molecular ion peak of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ is observed at 1495.95amu (calc. 1498.88). The base peak is observed at 800amu (100) (calc.801.48) due to the formation of $[Cu_2C_{21}H_{21}N_5O_{14}Cl_3]^+$. A medium peak at 1075.1amu (28.36) is due to the formation of $[Cu_2C_{31}H_{33}N_7O_{19}Cl_4]^+$. The mass spectrum of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ is given in fig.

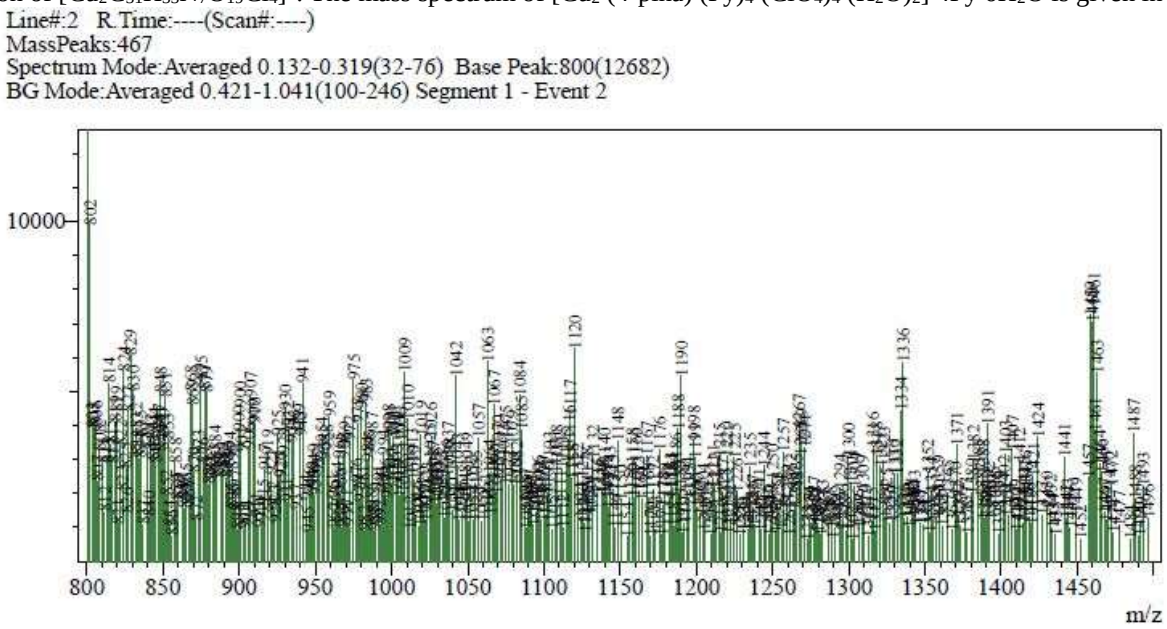


Fig.10. Mass spectrum of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$

## IV. APPLICATION

### A. Antimicrobial Activity

Antimicrobial activities are studied from Biogenix Research Centre, Thiruvananthapuram.

**i) Antibacterial Activity**

Antimicrobial studies was done by agar-well diffusion method in which the antimicrobials present in the samples are allowed to diffuse out into the medium (the medium was prepared by dissolving 33.8 g of the commercially available Muller Hinton Agar Medium (MHI Agar Media) in 1000ml of distilled water and it was autoclaved at 15 lbs pressure at 121°C for 15 minutes. The autoclaved medium was mixed well and poured onto 100mm petriplates (25-30ml/plate) while still molten) and interact in a plate freshly seeded with the test organisms the gram positive bacteria, *Staphylococcus aureus* (ATCC 25923) and the gram negative bacteria *Pseudomonas aeroginosa* (ATCC 27853) and E. Coli. Streptomycin was used as a positive control. The resulting zones of inhibition will be uniformly circular as there will be a confluent lawn of growth. The diameter of zone of inhibition can be measured in millimeters[10]. Concentration of stock 10mg/mL DMSO.

Table.6. Antibacterial activity, Zone of inhibition (mm) of ligands

| Complex | Concentration (µg/mL) | Pseudomonas aeroginosa | E Coli | Staphylococcus aureus |
|---|---|---|---|---|
| $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ | Streptomycin (100µg) | 25 | 20 | 28 |
| | 250 | NIL | NIL | 11 |
| | 500 | 11 | 12 | 11 |
| | 1000 | 13 | 15 | 13 |
| $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ | Streptomycin (100µg) | - | - | 23 |
| | 250 | - | - | NIL |
| | 500 | - | - | 11 |
| | 1000 | - | - | 16 |

Fig.11. Activity of $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ against the gram negative bacteria Pseudomonas aeroginosa

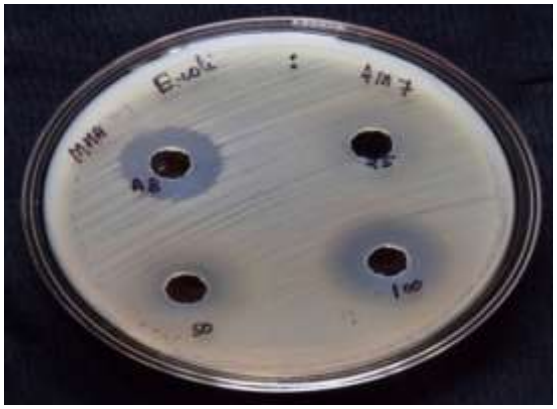

Fig.12. Activity of $[Cu_2(4\text{-pina})(Bpy)_2(ClO_4)_4(H_2O)_2]$ 2Bpy $6H_2O$ against the gram negative bacteria E.Coli.

Fig.13. Activity of $[Cu_2(4\text{-pina})(Bpy)_2(ClO_4)_4(H_2O)_2]$ 2Bpy $6H_2O$ against the gram positive bacteria Staphylococcus aureus

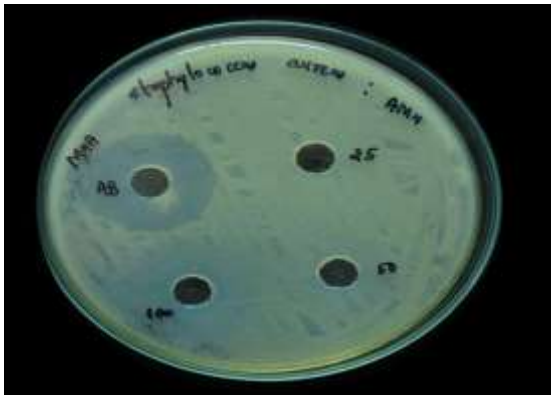

Fig.14. Activity of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]4Py6H_2O$ against the gram positive bacteria Staphylococcus aureus

From the results it was clear that the complex $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ was active against the gram negative bacteria Pseudomonas aeroginosa E Coli and the gram positive bacteria Staphylococcus aureus; whereas, $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]4Py$ $6H_2O$ was active against the gram positive bacteria Staphylococcus aureus.

**ii) Antifungal activity**

Antifungal activity was also done by agar-well diffusion method as described earlier, using the test organism *Candida albicans*(ATCC 10231). Clotrimazole (concentration: 10mg / ml) was used as a standard antifungal agent. The diameter of zone of inhibition can be measured in millimeters[11]. Concentration of stock 10mg/mL DMSO.

Table. 7. Activity of complexes against the fungus Candida albicans

| Sample | Concentration (µg/mL) | Zone of inhibition (mm) |
|---|---|---|
| $[Cu_2$ (4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ | Clotrimazole (100µg) | 19 |
| | 250 | 11 |
| | 500 | 12 |
| | 1000 | 15 |

From the results it was clear that$[Cu_2(4\text{-pina})$ $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ were active active against the fungus Candida albicans

Fig.15.Activity of $[Cu_2(4\text{-pina})$ $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ against the fungus Candida albicans

**iii). Minimum Inhibitory Concentration (MIC) Analysis[12]**

Minimum inhibitory concentration (MIC) is the lowest concentration of an anti microbial (like an antifungal antibiotic or bacteriostatic) drug that will inhibit the visible growth of a microorganism after overnight incubation. Minimal inhibitory concentration (MIC) was determined by using two fold serial dilution method. The growth of stock inoculum of test organisms (Pseudomonas aeruginosa, E.Coli or Staphylococcus aureus) was adjusted to 1% McFarland Standard. The broth dilution assay was done in 96 well microtiterplate. Each wells in the plate were added with 100µl of the diluted (two times) conidial inoculum suspensions (final volume in each well, 200 µl). Sample was dissolved in DMSO to a final concentration of 10mg/mL and was added in increasing concentration such as 62.5µg, 125µg, 250µg, 500µg, 1000µg to the wells respectively and incubated overnight at room temperature. A control well was kept with organism alone. Growth was observed by visual inspection and by measuring the optical density (OD) at 630 nm using an ELISA plate reader. The OD was measured immediately after the visual reading. The growth inhibition for the test wells at each extract dilution was determined by the formula:

Percentage of inhibition = (OD of control - OD of test)/ (OD of control) × 100

Table. 8. % Inhibition of complexes against test organisms

| Organism | OD at 630 nm | % Inhibition |
|---|---|---|
| Control, Pseudomonas aeruginosa | 0.63965 | 0 |
| conc. Of $[Cu_2$ (4-pina) $(Py)_4$ $(ClO_4)_4$ $(H_2O)_2]$ 4Py $6H_2O$ : 62.5µg | 0.1015 | 81.5135% |
| 125 µg | 0.0288 | 94.75% |
| 250 µg | 0.0193 | 96.5394% |
| 500 µg | 0.016 | 97.085% |
| 1000 µg | 0.0153 | 97.21336% |

**MIC = 54.0057 µg**

**B. Catalytic Activity**

Coordination complexes of 4-pina act as catalysts in a number of reactions. The catalytic activity was examined on the basis of decomposition reaction of hydrogen peroxide. The metal complex (~ $2X10^{-4}$ mmol) was mixed with 50ml of 10% $H_2O_2$ in a flask at room temperature under constant stirring. Then the extent of hydrogen peroxide decomposed at different intervals of time was estimated through permanganometry. 1ml aliquot of reaction mixture was withdrawn in each 30 minutes and titrated against 0.02M $KMnO_4$ in presence of 1:5 $H_2SO_4$ solution. The difference in titre values of permanganate solution before and after the catalysed decomposition was recorded[13, 14]

% decomposition of $H_2O_2$ = $(C_0-C_t/C_0)$ X 100

In presence of metallic complexes 37-39% of the decomposition reaction was found to be completed within 3hrs.

**i) Catalytic Activity of $[Cu_2(4\text{-pina})\ (Bpy)_2\ (ClO_4)_4\ (H_2O)_2]$ 2Bpy $6H_2O$**

Table.4.9. catalytic action of $[Cu_2$(4-pina) $(Bpy)_2$ $(ClO_4)_4$ $(H_2O)_2]$ 2Bpy $6H_2O$ in the decomposition reaction of hydrogen peroxide

| Time in minutes | Vol. Of $KMnO_4$ in ml | % decomposition |
|---|---|---|
| O | 78.4 | - |
| 30 | 72.7 | 7.27 |
| 60 | 71.6 | 8.67 |
| 90 | 68.4 | 12.76 |
| 120 | 62.8 | 19.9 |
| 150 | 52.0 | 33.67 |
| 180 | 49.1 | 37.37 |

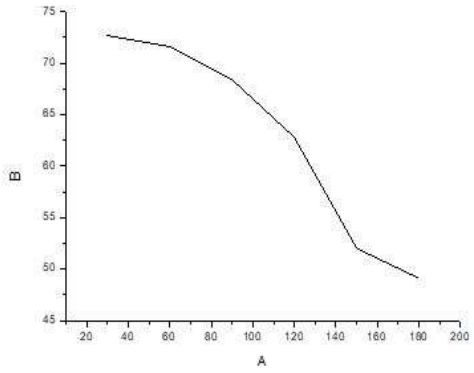


Fig.16. A-time in minutes; B-vol. of $KMnO_4$ in ml Fig..

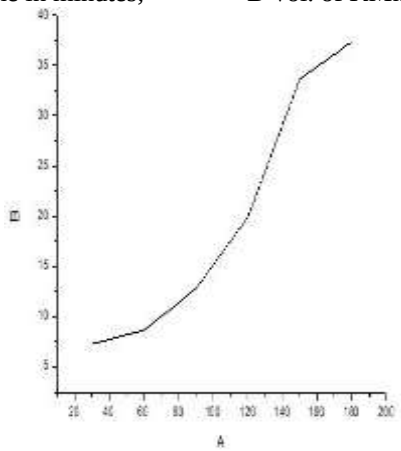


Fig.17-time in minute B-% decomp. $KMnO_4$ in ml of $H_2O_2$

**ii) Catalytic Activity of $[Cu_2(4\text{-pina})\ (Py)_4\ (ClO_4)_4\ (H_2O)_2]$ 4Py $6H_2O$**

Table.10. catalytic action of $[Cu_2(4\text{-pina})\ (Py)_4\ (ClO_4)_4\ (H_2O)_2]$ 4Py $6H_2O$ in the decomposition reaction of hydrogen peroxide

| Time in minutes | Vol. Of $KMnO_4$ in ml | % decomposition |
|---|---|---|
| O | 77.5 | - |
| 30 | 76,9 | 0.77 |
| 60 | 67.4 | 13.03 |
| 90 | 66.8 | 13.8 |
| 120 | 53.2 | 31.35 |
| 150 | 48.2 | 37.81 |
| 180 | 42.1 | 45.68 |

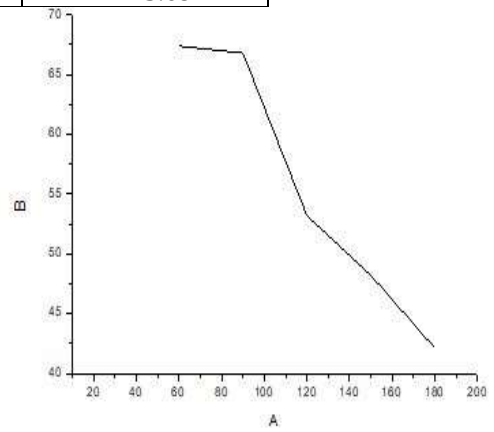


Fig.18. A-time in minutes; B-vol. of $KMnO_4$ in ml Fig..

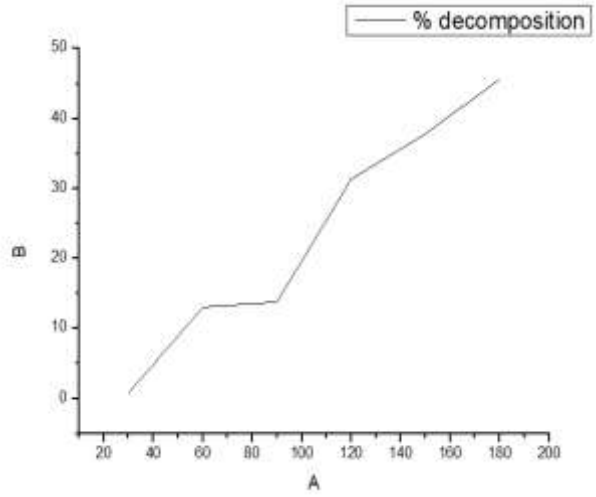


Fig. 19. A-time in minute B-% decomp. $KMnO_4$ in ml of $H_2O_2$

**C. Photocatalytic Activity**

Photocatalytic activity of complexes of 4-pina was examined on the basis of degradation reaction of methylene blue dye. The metal complexes (~0.01g) and aqueous solution of methylene blue (70ml) were mixed in a beaker under constant stirring at room temperature. The mixture was equilibrated by stirring in dark for thirty minutes to allow the adsorption of methylene blue dye, if any, by the complex. The solution is stirred under UV light. The sample was allowed to absorb UV light and 5ml aliquots were taken and filtered at a definite time interval of 30minutes. Filteration was done to avoid errors due to scattering of UV radiation. The filtrate was analysed using UV-Visible spectrophotometer. The intensity of the absorption peak of methylene blue at 663nm gets diminished gradually with extension of the exposure time indicating the degradation of methylene blue dye.

**i) Photocatalytic Activity of $[Cu_2(4\text{-pina})\ (Bpy)_2\ (ClO_4)_4\ (H_2O)_2]$ 2Bpy $6H_2O$**

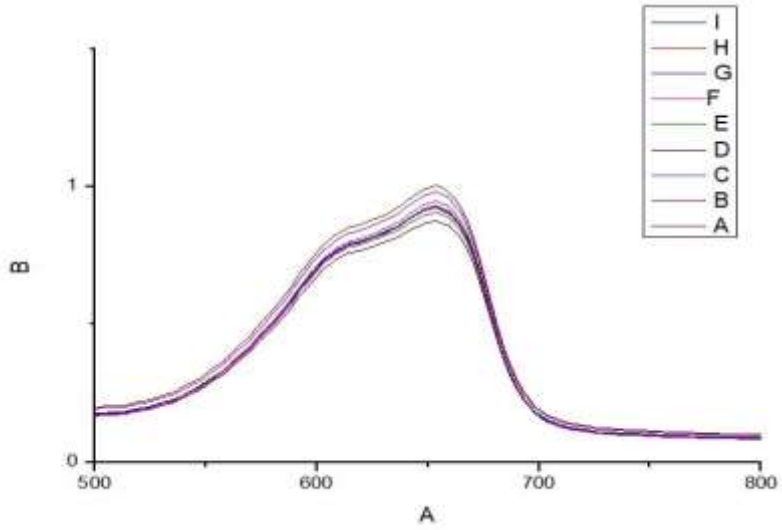


Fig.20. Photodegradation plot of methylene blue dye degradation under UV light using $[Cu_2(4\text{-pina})\ (Bpy)_2\ (ClO_4)_4\ (H_2O)_2]$ 2Bpy $6H_2O$ ; A- dark; B-0min; C-30min; D-60min; E-90min; F-120min; G Photodegradation plot of methylene blue dye degradation under UV light using $[Cu(dafone)_2\ (CH_3OH)_2]\ (ClO_4)_2$ ; A- dark; B-0min; C-30min; D-60min; E-90 min; F-120min; G-150min; H-180min; I-210 min;

## V. CONCLUSION

Complexes $[Cu_2\ (4\text{-pina})\ (Py)_4\ (ClO_4)_4\ (H_2O)_2]$ 4Py $6H_2O$ and $[Cu_2\ (4\text{-pina})\ (Bpy)_2\ (ClO_4)_4\ (H_2O)_2]$ 2Bpy $6H_2O$ were prepared by solvent based synthesise using methanol as solvent. All the complexes are binuclear. Characterisation of the ligand and complexes were done on the basis of various spectroscopic studies like $^1H$ nmr IR, UV, and mass spectroscopy. Its application as antimicrobial agent was studied with the test organisms like gram positive bacteria, Staphylococcus aureus (ATCC 25923); the gram negative bacteria Pseudomonas aeroginosa (ATCC 27853) and E.Coli; and the fungus Candida albicans. $[Cu_2\ (4\text{-pina})\ (Bpy)_2\ (ClO_4)_4\ (H_2O)_2]$ 2Bpy $6H_2O$ was active against the gram negative bacteria Pseudomonas aeroginosa and E. Coli. $[Cu_2\ (4\text{-pina})\ (Bpy)_2\ (ClO_4)_4\ (H_2O)_2]$ 2Bpy $6H_2O$ was moderately active against the gram negative bacteria E.Coli. Both the complexes are active against the gram positive bacteria, Staphylococcus aureus. $[Cu_2\ (4\text{-pina})\ (Py)_4\ (ClO_4)_4\ (H_2O)_2]$ 4Py $6H_2O$; was moderately active against the fungus Candida albicans. Its catalytic activity was studied by considering decomposition reaction of hydrogen peroxide and photocatalytic degradation of methylene bluedye. These complexes show moderate catalytical activity.

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