

# SYNTHESIS, SPECTRAL AND BIOLOGICAL STUDIES ON TRANSITION METAL COMPLEXES OF (Z)-2-(METHYLTHIO)-N-(PYRIDIN-2- YLMETHYLENE)ANILINE

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## ABSTRACT

The new Schiff base ligand (Z)-2-(methylthio)-N-(pyridin-2-ylmethylene)aniline MPMA derived from pyridine-2-carboxaldehyde and 2-(methylthio)aniline and its Cu(II), Co(II) and Zn(II) metal complexes were prepared and characterized by spectral, magnetic and electrochemical studies. The spectral studies revealed that the ligand MPMA was tridentate and coordinated to the metal through azomethine nitrogen atom, pyridine nitrogen atom and sulphur atom from amine, forming octahedral geometry for Cu<sup>2+</sup>, Co<sup>2+</sup> and tetrahedral geometry for Zn<sup>2+</sup> ions. It was further supported by molar conductance measurement, which indicated that the above-mentioned complexes 1 and 2 were formed in 1:2 metal-ligand ratio and complex 3 was formed in 1:1 metal-ligand ratio. The electrochemical study explored that the metal ions undergo quasi reversible redox reactions by two electron transfer processes. The bio-efficacy of the Schiff base and their metal complexes were studied in-vitro against the growth of microbes to assess their antimicrobial potential. The antioxidant activity of the ligand and the metal complexes have also been studied. The antidiabetic activity of the ligand and metal complexes were screened against  $\alpha$ -amylase enzyme and  $\alpha$ -glucosidase enzyme and compared with standard drug acarbose.

**Keywords:** Schiff base, Pyridine -2-Carboxaldehyde, 2-(Methylthio) Aniline, Acarbose, Antioxidant, Antidiabetic Activity.

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## INTRODUCTION

In the field of Organometallic Chemistry, Schiff base and its metal complexes have played a vital role due to their catalytic activity and biological activity such as antitumor, antimicrobial, anti-inflammatory, antidiabetic, anticancer, analgesics, pesticidal and antioxidant.<sup>1</sup> Depending upon the functional groups present, Schiff base can act as bidentate, tridentate, tetradentate or polydentate ligand and they readily form complexes with transition metal ions. A Schiff base is a nitrogen analogue of an aldehyde or ketone with an azomethine group in place of the carbonyl group. Schiff base chromophore has a large number of anharmonic phonons, which contribute significantly to their ability to coordinate with various ligands.<sup>2</sup> In recent years, metal-based medications have become increasingly significant in the medical field. Diabetes, cancer, inflammation, and cardiovascular disease were also treated. For the past ten years, transition metal complexes of Schiff base derived from Pyridine-2-carboxaldehyde have a lot of attention due to their synthetic and catalytic activities. Pyridine-2-carboxaldehyde Schiff base complexes have been quantified for their catalytic activities towards alkene epoxidation, hydrogenation, and hydroformylation.<sup>3</sup> Pyridine-2-carboxaldehyde Schiff base complexes and derivatives have also been recognized for High superoxide dismutase activities and found to be effective herbicides for the protection of plants.<sup>4</sup>

Encouraged by this information, we present the synthesis of Schiff base ligand (Z)-2-(methylthio)-N-(pyridine-2-ylmethylene)aniline derived from Pyridine-2-carboxaldehyde and 2-(Methylthio)Aniline and its metal complexes. The bio-efficacy of the free ligand and its complexes were tested in-vitro against

microbes with various dilutions in order to evaluate their antimicrobial potential. In addition, antioxidant and antidiabetic activities of the titled compounds were also studied.

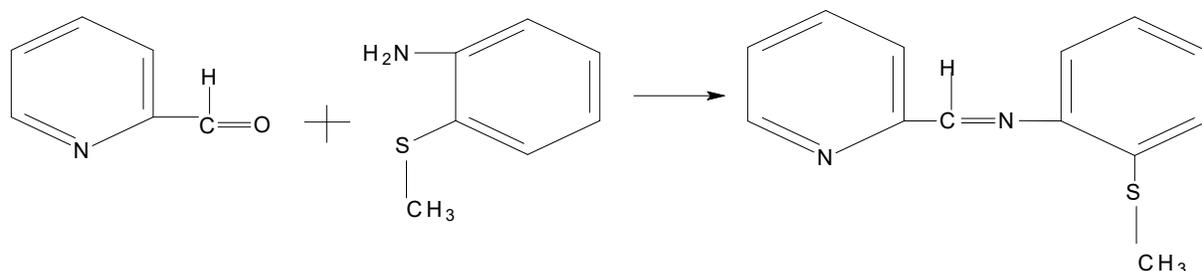
## EXPERIMENTAL

### Materials and Methods

The pyridine-2-carboxaldehyde and 2-methylthio aniline utilized for the preparation of ligand were obtained from Sigma-Aldrich. The metal salts were also obtained from Merck. Hence, all the substances were used without purification. The percentage of carbon, hydrogen, nitrogen and sulphur were performed on a Vario EL III CHNS analyser. IR spectra were recorded covering the range between 4000-250  $\text{cm}^{-1}$  on a Perkin Elmer Spectrum RX-I FTIR Spectrophotometer using KBr pellets. The  $^1\text{H}$ NMR spectrum of the ligand was recorded on the FT NMR Spectrometer Model Bruker Avance II at 400 MHz using DMSO as a solvent. Electronic spectra of ligand and metal complexes were recorded on an Elico SL164 double beam UV- Visible spectrophotometer between the range 200- 800nm in DMSO. Conductivity measurements of the prepared complexes were made on the freshly prepared  $10^{-3}\text{M}$  solution in DMF on an Equiptronics conductivity meter Model No. EQ 665 with a dip-type cell having a platinum electrode at room temperature. Cyclic Voltammetric measurements of all the prepared complexes were carried out using tetrabutylammonium perchlorate as supporting electrolyte on an HCH instruments version 5.01, model 600c series electrochemical analyzer. The three-electrode cell consists of a saturated calomel electrode as a reference electrode, platinum wire as a counter electrode, and glassy carbon as the working electrode.

### Synthesis of (Z)-2-(methylthio)-N-(pyridin-2-ylmethylene)aniline (Ligand)

An equimolar mixture of 2-methylthio aniline (20mmol) and pyridine-2-carboxaldehyde (20mmol) in ethanol (25ml) was refluxed for about 6 to 7 hours on a water bath. Dark brown coloured product (L) separated in hot was filtered off, rinsed with cold ethanol and dried in a desiccator over anhydrous calcium chloride.



(Z)-2-(methylthio)-N-(pyridin-2-ylmethylene)aniline.  
Scheme-1: Synthesis of (Z)-2-(methylthio)-N-(pyridin-2-ylmethylene)aniline

### Synthesis of Metal Complexes

(Z)-2-(methylthio)-N-(pyridin-2-ylmethylene)aniline (20mmol) in 20 ml of absolute ethanol was added dropwise to a solution containing metal salts (10mmol) in 20 ml of absolute ethanol. The mixture was refluxed for 2-5 hours on a water bath. The precipitate obtained was rinsed with cold ethanol and dried in a desiccator over anhydrous calcium chloride. The metal salts used were Copper Chloride Dihydrate and Cobalt Nitrate Heptahydrate.

(Z)-2-(methylthio)-N-(pyridin-2-ylmethylene)aniline (10mmol) in 20 ml of absolute alcohol was added dropwise to a solution containing zinc sulphate heptahydrate (10mmol) in 20 ml of ethanol solution. The mixture was refluxed for 3 to 6 hours on a water bath. The precipitate obtained was rinsed with cold ethanol and dried in a desiccator over anhydrous calcium chloride.

### In-vitro Antibacterial Activity

Muller Hinton agar mediums were used to screen the newly synthesized ligand and its metal complexes for antibacterial activity using the agar well dilution method. The in-vitro antibacterial activity of the test compounds was tested against two gram-positive bacteria and one gram-negative bacteria. Base plates were prepared by pouring 20 ml of autoclaved Muller Hinton agar into sterilized petri dishes and allowing them

to settle. A broth culture of *B.subtilis*, *S.aureus*, and *E.coli* bacteria was incubated with molten autoclaved Muller Hinton agar that had been maintained at 38<sup>0</sup> C for 15 minutes for adsorption. Wells were drilled into the seeded agar plates with a sterile cork borer of 8mm diameter, and these wells were injected with test chemical solutions. The stock solution of each test compound was prepared by dissolving 10mg of each test compound in 10ml of freshly distilled DMSO. Further various concentrations of the compounds (100, 75, 50, 25 μL) were prepared by diluting the stock solution with the required volume of distilled DMSO. All the plates were incubated at 38<sup>0</sup> C for 24 hours and the zone of inhibition was measured around each disc. As these organisms grow, it develops a turbid layer except in the region where the concentration of antibacterial agent is above Minimum Inhibition Concentration MIC and a zone of inhibition is observed. The diameter of the inhibition zone depends upon the culture medium, rate of diffusion, concentration of antimicrobial agent and incubation condition. Gentamicin is used as a reference. For each organism, the procedure was repeated three times on three replicate plates.

### ***In-vitro* Antifungal Activity**

Potato dextrose media were used to screen the newly synthesised ligand and its metal complexes for antifungal activities by agar well dilution method. Antifungal activity was carried out against *Pseudomonas aeruginosa*, *Candida albicans*, *Aspergillus niger*. Base plates were prepared by pouring 20ml of autoclaved Potato dextrose into sterilized Petric dishes and allowing them to settle. Molten autoclave potato dextrose that has been maintained at 38<sup>0</sup>C was incubated with the broth culture of *Pseudomonas aeruginosa*, *Candida albicans*, *Aspergillus niger* and kept for 15 minutes for adsorption. Wells were bored into the seeded dextrose plates using sterile cork borer of 8 millimetre diameter, and these wells were loaded with the test compounds solutions. Stock solution of each test compounds was prepared by dissolving 10mg of each test compounds in 10 ml of freshly distilled DMSO. Further various concentration of the test compounds (100, 75, 50, 25 μL) was prepared by diluting the stock solution with the required volume of distilled DMSO. Plates were incubated at 38<sup>0</sup>C for 24 hours and the zone of inhibition was measured around each disc. As these organisms grow, it forms a turbid layer except in the region where the concentration of the antifungal agent is above MIC and a zone of inhibition is seen. Ketoconazole is used as a reference. For each organism, the procedure was repeated three times on three replicate plates.

### **Antioxidant Activity (Free radical Scavenging Activity)**

2,2 -diphenyl -1-picryl hydrazyl (DPPH) assay was used for determining the free radical scavenging activity of the Schiff base ligand and its metal complexes. 0.9 ml of 1.5x10<sup>-4</sup> M DPPH radical solution in methanol should be prepared and mixed with different concentrations of test samples (5,10,15,20 μL) and to the standard L-ascorbic acid that was taken in different test tube and volume of each test tube was adjusted to 100 μL by adding DMSO and kept in the dark for 30 minutes. The quantity of DPPH remaining in the mixed solution should be measured at 520nm. The reduction in the absorbance of the DPPH solution indicates the free radical scavenging activities of the test samples. Methanol without the sample should be used as a control. The DPPH radical scavenging activity will be calculated according to the following formula.

$$\% \text{ Inhibition Ratio} = \frac{[\text{Abs}_{\text{control}} - \text{Abs}_{\text{sample}}]}{[\text{Abs}_{\text{control}}]} \times 100.$$

### **Antidiabetic Activity**

#### **Alpha -Amylase Inhibitory Assay**

Using the synthesized silver nanoparticles, the Alpha - amylase inhibitory experiment was performed. In a test tube, 250μL of sample solution (20-100g/ml) was added, followed by 250μL of 0.02 M sodium phosphate buffer (pH 6.9) containing Alpha - amylase solution (0.5 mg/ml). The solution was pre-incubated for 10 minutes at 25<sup>0</sup> C, after which 250 μL of 1% starch solution in 0.02M sodium phosphate buffer (pH 6.9) was added at regular intervals and incubated for another 10 minutes at 25<sup>0</sup> C. The reaction gets terminated by the addition of 500 μL of Dinitro salicylic acid (DNS) reagent. The tubes were then incubated in boiling water for 5 minutes and cooled at room temperature. The reaction mixture was diluted by adding 5 ml distilled water and the absorbance was measured at 540nm using spectrophotometer .A control was

prepared using the same procedure by replacement of the sample solution with distilled water. The Alpha - amylase inhibitory activity was calculated in terms of percentage.

$$\% \text{ Inhibition Ratio} = \frac{[\text{Abs}_{\text{control}} - \text{Abs}_{\text{sample}}]}{[\text{Abs}_{\text{control}}]} \times 100$$

#### Alpha- Glycosidase Inhibitory Assay

The activity of sample solution on  $\alpha$ -glucosidase was determined by using  $\alpha$ -glucosidase from *saccharomyces cerevisiae*. p-nitro phenol glucopyranoside (p-NPG) was prepared in 20mM phosphate buffer as a substrate solution and pH 6.9. 100 $\mu$ L of  $\alpha$ -glucosidase (1.0 U/ mL) was pre-incubated with 50  $\mu$ L of the different concentration (20-100  $\mu$ g/ml) of the sample solutions for 10 minutes. Then 50  $\mu$ L of 3.0 mM (p-NPG) substrate was dissolved in 20 mM Phosphate buffer (pH 6.9) were added to initiate the reaction. The reaction mixture was incubated at 37°C for 20 min and stopped by adding 2 ml of 0.1M sodium carbonate. The  $\alpha$ -glucosidase activity was determined by measuring the yellow colour p- nitro phenol released from p-NPG at 405nm. The results were expressed in the percentage of the blank control. The Alpha glucosidase inhibitory activity was calculated by percentage inhibition.

$$\% \text{ Inhibition Ratio} = \left[ \frac{\text{Abs}_{\text{control}} - \text{Abs}_{\text{sample}}}{\text{Abs}_{\text{control}}} \right] * 100$$

### RESULTS AND DISCUSSION

The analytical data and some physical properties of the ligand MPMA and its metal complexes 1-3 were noted in Table-1. The data showed that the Copper (II) and Cobalt (II) complexes were formed in the ratio 1:2 (M: L) whereas Zinc (II) complex was formed in the ratio 1:1 (M: L). The resulting metal complexes 1-3 were found to be solid, non-hygroscopic, stable at room temperature. These complexes 1-3 were soluble in DMF, DMSO and insoluble in common solvents like water, ethanol, and methanol. The purity of ligand MPMA and the complexes 1-3 were checked by Thin Layer Chromatography using silica gel-G as adsorbent. Conductivity measurements in the DMF solvent showed that the Complexes 1 and 2 were electrolytes in nature whereas complex 3 was non-electrolyte in nature. The ligand MPMA and Complexes 1-3 gave a sharp melting point indicating the separation of fairly pure compounds.

Table-1: Analytical Data and Physical Properties of the Ligand MPMA and Metal Complexes

Compounds	Empirical Formula	Colour	M. Wt. g.mol <sup>-1</sup>	Melting Point °C	Elemental Analysis (%) Found (Cal)			
					C	H	N	S
MPMA	C <sub>13</sub> H <sub>12</sub> N <sub>2</sub> S	Brown	228.32	209	68.39 (68.41)	5.29 (5.25)	12.27 (12.21)	14.04 (14.08)
[Cu(MPMA) <sub>2</sub> ].Cl <sub>2</sub>	CuC <sub>26</sub> H <sub>24</sub> N <sub>4</sub> S <sub>2</sub>	Dark Green	520.17	>250	59.96 (60.10)	4.65 (4.69)	10.77 (10.71)	12.33 (12.29)
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	CoC <sub>26</sub> H <sub>24</sub> N <sub>4</sub> S <sub>2</sub>	Brown	515.55	>250	60.57 (60.59)	4.69 (4.71)	10.86 (10.83)	12.44 (12.48)
[Zn(MPMA)S O <sub>4</sub> ]	ZnC <sub>13</sub> H <sub>12</sub> N <sub>2</sub> S <sub>2</sub> O <sub>4</sub>	Dirty White	389.75	>250	40.06 (40.08)	3.10 (3.09)	7.19 (7.21)	16.45 (16.41)

#### <sup>1</sup>H NMR Spectra

The <sup>1</sup>H NMR spectra of the ligand were recorded in DMSO, the Ar-H were resonated as a multiplet signal in the range 6.2- 7.1  $\delta$  ppm. The sharp singlet peak in the region 8.3  $\delta$  ppm was due to the azomethine proton. The methyl group protons appear as a singlet at 2.3  $\delta$  ppm.<sup>5,6</sup>

#### Infrared Spectra

IR Spectroscopy is an appropriate technique to provide enough information to interpret the mode of binding of the ligand to the metal ion. The identification of the coordinating atoms was made on the basis of a comparison of the IR spectra of ligand and the complexes.

The free Schiff base ligand MPMA showed a strong band at 1673 cm<sup>-1</sup>, which was the characteristic band of azomethine linkage (-CH=N). On complexation of the ligand to metal ions through the azomethine

linkage reduces the electron density around the nitrogen atom, which lowers the  $\nu_{(-CH=N)}$  absorption frequency. The band due to azomethine linkage was now moved to lesser frequencies in the spectra of all complexes 1-3 (1621cm<sup>-1</sup> to 1626cm<sup>-1</sup>), signifying the coordination of azomethine nitrogen to metal ions. The coordination of azomethine nitrogen to metal ions was further supported by the presence of bands in the region of 482- 497 cm<sup>-1</sup> which were due to M-N linkage.<sup>7</sup>

In the spectra of the ligand MPMA, the band at 1585cm<sup>-1</sup> was due to  $\nu_{(-CH=N)}$  stretching vibration of pyridine ring. This band in the spectra of all complexes 1-3 were shifted to lower frequencies (1435-1496 cm<sup>-1</sup>), indicating the coordination of this group to the metal ions.<sup>8</sup>

Bands in the range (656-645cm<sup>-1</sup>) confirmed the coordination of sulphur atoms to the metal ions.<sup>8</sup> The presence of very sharp bands in the range (564-602cm<sup>-1</sup>) indicated the formation of M-N bond involving nitrogen atom of pyridine ring.<sup>9</sup>

This information suggested that the ligand coordinates to the metal ions in tridentate fashion.

### Electronic Spectra

The electronic spectrum of the synthesized ligand MPMA and complexes 1-3 were recorded at room temperature using DMSO solvent. The spectrum of the Schiff base ligand shows two absorption bands at 35,087cm<sup>-1</sup> and 24,390cm<sup>-1</sup>, which were due to  $\pi-\pi^*$  and  $n-\pi^*$  transition of the azomethine group of ligand and this transition were shifted to a longer wavelength in the spectrum of the complexes indicating the coordination of ligand to metal through azomethine moiety. Electronic spectrum of Copper (II) complexes show three absorption bands in their region 28,089cm<sup>-1</sup>, 20,833cm<sup>-1</sup> and 16,260cm<sup>-1</sup> which were assigned to  ${}^2B_{1g} \rightarrow {}^2E_g$ ,  ${}^2B_{1g} \rightarrow {}^2B_{2g}$ , d-d transition respectively. These values suggested distorted octahedral geometry. The magnetic moment of the Copper (II) complex was 1.98 BM which confirmed an octahedral geometry.<sup>10,11</sup>

For Cobalt (II) complex, three absorption bands were observed in the range 13,458 cm<sup>-1</sup>, 16,650 cm<sup>-1</sup>, and 21,834 cm<sup>-1</sup>, which corresponds to three spin allowed transitions  ${}^4T_{1g(F)} \rightarrow {}^4T_{2g(F)}$ ,  ${}^4T_{1g(F)} \rightarrow {}^4A_{2g(F)}$ ,  ${}^4T_{1g(F)} \rightarrow {}^4T_{2g(P)}$  respectively. The magnetic moment of Cobalt (II) complexes at room temperature were 4.80 BM which confirmed an octahedral geometry.<sup>12</sup>

Zinc (II) complex showed only one band, centered at 36,363 cm<sup>-1</sup> was attributed to metal-ligand charge transfer, which was well-matched with this complex possessing a tetrahedral geometry.<sup>13,14</sup>

### Cyclic Voltammetry

Cyclic voltammetry studies of the synthesized complexes 1-3 were investigated in DMF (10<sup>-3</sup>mol<sup>-1</sup>) at the scan rate of 0.01V in the potential range from + 2 V to -2 V. The redox potential were summarised in the Table-2. The  $\Delta E_p$  values lie from 206-245mV. The ratio of  $I_{pa}/I_{pc}$  of all the complexes falls around 1.65, which is a sign of one two-electron transfer process. Thus from the above observations, it was clear that the above-mentioned mononuclear metal complexes undergo one two-electron quasi reversible reduction.<sup>15</sup>

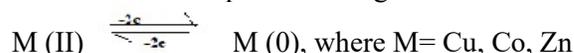


Table-2: MRedox Potentials for Metals (II) Complexes in DMF Solution at 298 K.

Complex	$E_{pc}$ (mV)	$E_{pa}$ (mV)	$\Delta E_p$ (mV)	$i_{pc}$ ( $\mu A$ )	$i_{pa}$ ( $\mu A$ )	$i_{pa}/i_{pc}$
Cu(MPMA) <sub>2</sub> .Cl <sub>2</sub>	- 42.93	203.96	246.89	69.38	113.72	1.62
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	-10.12	196.59	206.71	73.71	118.16	1.60
[Zn(MPMA)SO <sub>4</sub> ]	-30.66	200.27	230.93	59.66	98.6	1.65

### Antibacterial Activity

The ligand MPMA and its metal complexes 1-3 were screened against two gram-positive bacteria such as *B.subtilis* and *S.aureus* and one gram-negative bacteria such as *E.coli* to study their antibacterial properties. The results represent Cobalt (II) complex possesses the highest activity against three bacterial species, followed by Copper (II) and Zinc (II) complexes which showed moderate activity compared to the ligand. The Cobalt (II) complex exhibited 36mm, 30mm, and 32mm zone of inhibition against *B.subtilis*, *S.aureus* and *E.coli*, respectively where these values are greater than the ligand MPMA as well as the control gentamicin.<sup>16</sup> The outcomes are shown in Table-3.

Table-3: Antibacterial Activity Data of Ligand MPMA and Metal Complexes

Ligand and Complexes	<i>B.subtilis</i>	<i>S.aureus</i>	<i>E.coli.</i>
MPMA	20	17	18
[Cu(MPMA) <sub>2</sub> ].Cl <sub>2</sub>	28	22	32
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	36	30	32
[Zn(MPMA)SO <sub>4</sub> ]	20	24	22
GENTAMICIN	20	20	20

### Antifungal Activity

The in-vitro antifungal activity of synthesized ligand MPMA and the complexes 1-3 were studied against *P.aeruginosa*, *C.albicans* and *A.niger*. Copper (II) complex was found to possess high activity towards *A.niger*, whereas Cobalt (II) complex exhibits high activity towards *P.aeruginosa* and *C.albicans*.<sup>17</sup> The results were exposed in the Table-4.

Table-4: Antifungal Activity Data of Ligand MPMA and Metal Complexes

Ligand and Complexes	<i>P. aeruginosa</i>	<i>C. albicans</i>	<i>A.niger</i>
MPMA	14	16	15
[Cu(MPMA) <sub>2</sub> ].Cl <sub>2</sub>	26	27	36
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	32	28	32
[Zn(MPMA)SO <sub>4</sub> ]	20	22	30
Ketoconazole	20	20	20

### Antioxidant Activity

The antioxidant activity of synthesized ligand MPMA and its metal complexes 1-3 were tested by DPPH method. DPPH is a stable free radical that can receive an electron or hydrogen radical to form a stable diamagnetic molecule. DPPH has an odd electron and so has a strong absorption band at 517 nm. When this electron becomes paired off, the absorption decreases stoichiometrically with respect to the number of electrons or hydrogen atoms are taken up. Such a decrease in absorbance increases the scavenging activity of the compounds. This tendency of decrease in absorption increases with increases in the concentration of the test compounds. The results in Table-5 suggested that the Zinc (II) complex possesses high antioxidant activity and shows promise for further investigation to target oxidative damage disease.<sup>18</sup>

Table-5: Antioxidant Activity Data of Ligand MPMA and Metal Complexes

Ligand and Complexes	% of Inhibition			
	5.0μL	10μL	15μL	20μL
MPMA	10	12	15	18
[Cu(MPMA) <sub>2</sub> ].Cl <sub>2</sub>	27	36	41	48
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	13	21	36	42
[Zn(MPMA)SO <sub>4</sub> ]	29	40	44	49
L-Ascorbic acid	49	52	59	64

### Antidiabetic Activity

In this study, the inhibitory effect of Schiff base ligand MPMA and its metal complexes 1-3 on carbohydrate hydrolyzing enzyme alpha amylase and alpha glucosidase was studied. The results of antidiabetic activity are shown in Table-6 and Table-7. These enzyme inhibitors work by inhibiting the action of these enzymes and delaying carbohydrate digestion, preventing a rapid rise in blood glucose levels, particularly after meals. Therefore inhibition of these two enzymes is a promising strategy for diabetes management. Metal complexes 1-3 were found to exhibit more inhibition efficiency than the ligand MPMA and comparable or slightly less efficiency than the standard drug acarbose.

Cobalt (II) complex showed excellent inhibition efficiency against Alpha amylase enzyme and Copper (II) complex exhibited high inhibition efficiency towards Alpha glucosidase enzyme.

The enhanced activity of the Cobalt (II) complex was due to the tendency of Cobalt to lower the glycemic level and act as an effective agent for diabetes. The enhanced activity of copper (II) complex against

diabetes was due to the tendency of copper to increase the tolerance of pancreatic  $\beta$ -cells against oxidative stress.

The enhanced activity of Zinc (II) complex was due to the fact that Zinc has an insulin mimetic effect and defends against oxidative damage linked with the disease for the treatment of diabetes mellitus.<sup>19,20</sup>

Ligand and Complexes	% of Inhibition				
	20 $\mu$ g/ml	40 $\mu$ g/ml	60 $\mu$ g/ml	80 $\mu$ g/ml	100 $\mu$ g/ml
MPMA	29.13	33.71	39.65	43.70	47.08
[Cu(MPMA) <sub>2</sub> ].Cl <sub>2</sub>	45.80	51.44	55.64	59.79	63.78
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	53.82	59.66	63.82	71.44	75.73
[Zn(MPMA)SO <sub>4</sub> ]	51.29	56.78	62.21	68.53	73.64
Acarbose	66.90	72.53	77.46	81.69	85.21

Ligand and Complexes	% of Inhibition				
	20 $\mu$ g/ml	40 $\mu$ g/ml	60 $\mu$ g/ml	80 $\mu$ g/ml	100 $\mu$ g/ml
MPMA	24.17	28.67	31.53	38.92	46.76
[Cu(MPMA) <sub>2</sub> ].Cl <sub>2</sub>	53.63	57.80	63.45	66.09	70.91
[Co(MPMA) <sub>2</sub> ].NO <sub>3</sub>	43.27	51.54	58.63	63.42	67.28
[Zn(MPMA)SO <sub>4</sub> ]	48.63	56.91	61.73	65.41	68.81
Acarbose	73.63	77.27	80	82.72	85.45

### CONCLUSION

Three new complexes, Copper (II), Cobalt (II) and Zinc (II) with a tridentate NNS - donor Schiff base ligand MPMA resulting from pyridine -2 -carboxaldehyde and 2-(methylthio)aniline were prepared and characterized by NMR, IR, UV-Visible, Cyclic Voltammetry and tested for antimicrobial, antioxidant and antidiabetic activity. The result demonstrated that copper (II) and Cobalt (II) complexes possess distorted +octahedral geometry and Zinc (II) complex show tetrahedral geometry. Antimicrobial, antioxidant and antidiabetic activities reveals that the metal complexes were more active than the Schiff base ligand which is in agreement with the fact that chelation of metals to the ligand enhances the biological activity of the Complexes.

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