



## Synthesis, spectral studies, XRD, thermal analysis and biological screening of metal complexes derived from (N-(3-methoxyphenyl)-2-[(2E)-3-phenylprop-2-enoyl] hydrazinecarboxamide

T. C. M. Yuvaraj<sup>1</sup>, P. Parameshwara Naik<sup>1\*</sup>, T.V. Venkatesh<sup>2</sup>, G. Krishnamurthy<sup>1</sup> and T. Manjuraj<sup>1</sup>.

<sup>1</sup>Department of Chemistry, S.S.College (Auto), Shivamogga, Karnataka (INDIA).

<sup>2</sup>Department of Chemistry, Shankaragatta, Kuvempu University, Karnataka (INDIA).

**Abstract:** Complexes of nickel(II), cobalt(II), copper(II), zinc(II), and manganese(II) are derived from the ligand, (N-(3-methoxyphenyl)-2-[(2E)-3-phenylprop-2-enoyl]hydrazinecarboxamide [MPH] and structurally characterized by various physicochemical and spectral tools such as FTIR, UV-Visible, <sup>1</sup>H NMR, LC-Mass, P-XRD and TGA-DTC. These studies showed that the ligand coordinated to the 3d metal ions in bidentate manner. X-ray diffraction studies indicates that the Ni(II), Cu(II) and Zn(II) complexes are crystalline in nature. Degradation mechanisms, thermodynamic and kinetic parameters of the synthesized metal complexes have been evaluated. The prepared ligand and complexes were evaluated for *in-vitro* antioxidant DPPH assay, in which metal complexes showed excellent activity. The molecular docking analysis by using human antioxidant enzyme *DTT* (*PDB: 3MNG*) have also been evaluated. The ligand and their metal complexes were screened for their antimicrobial activities against different pathogenic bacterial and fungal species.

**Keywords:** Semicarbazide, Metal complexes, P-XRD, TGA, antioxidant, Molecular docking.

**Submitted:** December 03, 2017. **Accepted:** June 30, 2018.

**Cite this:** 1. Yuvaraj T, Parameshwara Naik P, Venkatesh T, Krishnamurthy G, Manjuraj T. Synthesis, spectral studies, XRD, thermal analysis and biological screening of metal complexes derived from (N-(3-methoxyphenyl)-2-[(2E)-3-phenylprop-2-enoyl] hydrazinecarboxamide. JOTCSA. 2018;5(2):845-56.

**DOI:** <http://dx.doi.org/10.18596/jotcsa.341379>.

**\*Corresponding author.E-mail:** [parashchem@gmail.com](mailto:parashchem@gmail.com).

### INTRODUCTION

Semicarbazide and its derivatives are reported to be pharmacologically and physiologically active and find various applications in the treatment of several diseases (1-2). These are biologically active and are nontoxic due to the presence of ureido unit (-NH-CO-NH-NH-), which acts as pseudodipeptide motif. The derivatives of semicarbazone are an important class of ligand containing nitrogen and oxygen as donor atoms. The chemistry of the transition metal complexes of semicarbazone became largely appealing because of their extensive profile of medicinal and pharmacological activity that provides a variety of compounds with diverse applications (3-5). The semicarbazone derivatives and their transition metal complexes

show variable bio-potential activities like antibacterial, antifungal, antiarthritic, antimalarial, antitumor, antiviral, and anti-HIV agents and they have been well documented in the literature (6-7). The above important applications of semicarbazone derivatives and their 3d metal complexes in various fields prompted us to synthesize some derivatives of semicarbazone and their complexes to enhance their activities and test against *mycobacterium tuberculosis* (8-9). Now we report the synthesis, characterization, and biological activities of transition metal complexes containing amide-appended (2E)-3-phenylprop-2-enehydrazide and 1-isocyanato-3-methoxybenzene. This ligand system coordinates with the metal ion in a bidentate manner through the carbonyl oxygen and azomethine nitrogen (10). The aim of the

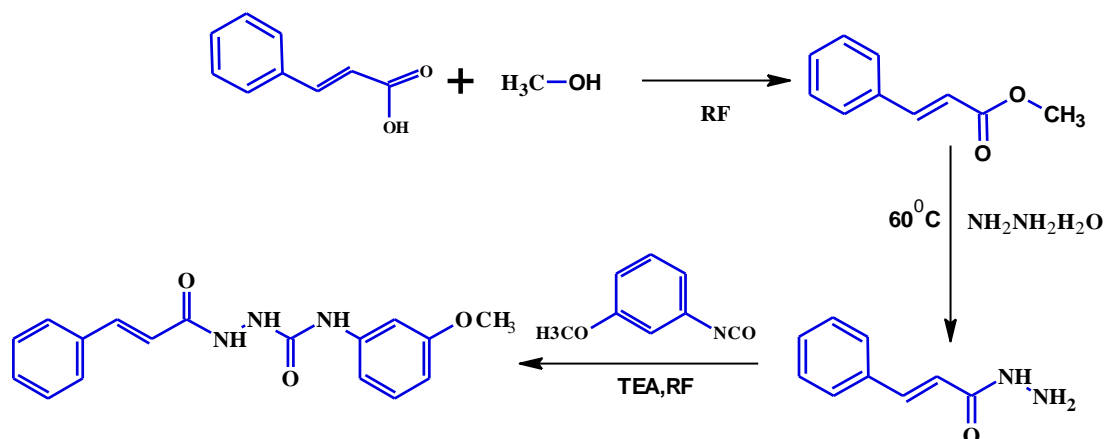
present work deals specifically the coordination properties of *N*-(3-methoxyphenyl)-2-[(*E*)-3-phenylprop-2-enoyl]hydrazinecarboxamide concerning its interactions with Ni(II), Co(II), Cu(II), Zn(II) and Mn(II) complexes, spectral characterization and thermal decomposition studies serve as important tools for the interpretation of structures of molecules and also biological and analytical importance. molecular docking study have been performed to investigate the interaction and binding energies of the complexes with protein enzyme by using HEX 8.2 for antioxidant activity, the compounds were also performed to investigate against the growth of *in-vitro* bacteria and pathogenic fungi.

## MATERIALS AND METHODS

The chemicals cinnamic acid, 1-isocyanato-3-methoxybenzene, hydrazine hydrate, and methanol were purchased from Sigma Aldrich, Laboratory chemicals, Bangalore, Karnataka, India. Nickel(II) chloride hexahydrate, cobalt(II) chloride hexahydrate, copper(II) chloride hexahydrate, anhydrous zinc(II) chloride and manganese(II) chloride were purchased from Merck. The metal chlorides were used in their hydrated form. The solvents were distilled and dried by standard method.

## Synthesis of *N*-(3-methoxyphenyl)-2-[(*E*)-3-phenylprop-2-enoyl]hydrazinecarboxamide (MPH)

A mixture of cinnamic acid (2.96 g, 0.02 mol) and 5 drops of conc. H<sub>2</sub>SO<sub>4</sub> in 30 mL of dry methanol was refluxed for 8 hours. The solvent was evaporated under reduced pressure. The white solid methyl (*E*)-3-phenylprop-2-enoate formed was filtered and recrystallized from a mixture of ethanol and acetone in the ratio 1:2. The mixture of methyl (*E*)-3-phenylprop-2-enoate (3.24 g, 0.02 mol) and hydrazine hydrate (1.10 g, 0.022 mol) in 20 mL of dry methanol was refluxed for 6 hours and the resulting mixture was evaporated under vacuum. The white solid, (*E*)-3-phenylprop-2-enehydrazide formed was filtered off, washed with water, dried and recrystallized from dioxane. Then, the solution of (*E*)-3-phenylprop-2-enehydrazide (3.23 g, 0.02 mol), 1-isocyanato-3-methoxybenzene (2.98 g, 0.02 mol) and triethylamine (0.51 g, 0.005 mol) in 40 mL of dry methanol was added and refluxed for about 10 hours. The reaction mixture was poured into ice-cold water. The cream colored solid of *N*-(3-methoxyphenyl)-2-[(*E*)-3-phenylprop-2-enoyl]hydrazinecarboxamide formed was filtered and recrystallized from ethanol.



**Scheme 1:** Synthesis of the ligand MPH.

C<sub>17</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>: Yield: 78%; Color: Cream; M.p: 122-124 °C; Mol.wt: 311.33; Elemental analyses: calculated and found (%): C: 65.58 (65.99), H: 5.50 (5.72), N: 13.50 (13.69), O: 15.42; IR (KBr, cm<sup>-1</sup>): 3182 (NH<sup>9</sup>), 3243 (NH<sup>12</sup>), 3320 (NH<sup>13</sup>), 2943 (Ar-CH), 1709 (C=O<sup>10</sup>), 1665 (C=O<sup>14</sup>), 1014 (N-N), 1604 (Ar-OCH<sub>3</sub>), 1207 (CH<sup>16</sup>=CH<sup>17</sup>). <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz): δppm 8.24 (s, 1H, NH<sup>9</sup>), 8.84 (s, 1H, NH<sup>12</sup>), 9.99 (s, 1H, NH<sup>13</sup>), 7.16 (s, 1H, Ar-H<sup>2</sup>), 6.56, 7.25 (d, 2H, Ar-H<sup>4,6</sup>), 7.13 (t, 1H, Ar-H<sup>5</sup>), 3.71 (s, 3H, OCH<sub>3</sub>), 7.62, 7.61 (d, 2H, Ar-H<sup>19,23</sup>), 7.39-7.45 (t, 3H, Ar-H<sup>20,21,22</sup>); Mass of the ligand M<sup>+</sup> at m/z: 312.00.

## Synthesis of the metal complexes

A solution of nickel(II) chloride hexahydrate (0.950 g, 0.004 mol), cobalt(II) chloride

hexahydrate (0.951 g, 0.004 mol), copper(II) chloride dihydrate (0.697 g, 0.004 mol), zinc(II) chloride (0.545 g, 0.004 mol) and manganese(II) chloride tetrahydrate (0.692 g, 0.004 mol) in 20 mL of ethanol was added one each time to the solution of *N*-(3-methoxyphenyl)-2-[(*E*)-3-phenylprop-2-enoyl]hydrazinecarboxamide (1.245 g, 0.004 mol) in 20 mL of ethanol. The resulting reaction mixture was refluxed for about 10 hours. The solid product was collected by filtration and washed with 4-5 mL of hot water and dried under vacuum over anhydrous calcium chloride in desiccator.

(i) [Ni(MPH)<sub>2</sub>Cl<sub>2</sub>].H<sub>2</sub>O: C<sub>34</sub>H<sub>32</sub>Cl<sub>2</sub>N<sub>6</sub>NiO<sub>6</sub>.H<sub>2</sub>O: Yield: 68%; Color: Dark brown; M.p: 280-282 °C; Mol. wt: 768.25; Elemental analyses:

calculated and found (%): C: 54.43 (54.64), H: 4.30 (4.80), N: 11.20 (11.48); IR (KBr,  $\text{cm}^{-1}$ ): 3441 ( $\text{H}_2\text{O}$ ), 3168 ( $\text{NH}^9$ ), 3056 ( $\text{NH}^{12}$ ), 1592 ( $\text{C}=\text{O}^{10}$ ), 1504 ( $\text{C}=\text{O}^{14}$ ), 1218 (N-N), 1504 (A-OCH<sub>3</sub>), 1218 (CH=CH), 448 (M-O), 422 (M-N); Molar conductance: 15.72  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ .

**(ii) [Co(MPH)<sub>2</sub>Cl<sub>2</sub>]:**  $\text{C}_{34}\text{H}_{32}\text{Cl}_2\text{CoN}_6\text{O}_6$ : Yield: 62%; Color: Gray; M.p: 253-254 °C; Mol.wt: 750.49; Elemental analyses: calculated and found (%): C: 54.41 (54.61), H: 4.30 (4.44), N: 11.20 (11.32); IR (KBr,  $\text{cm}^{-1}$ ): 3159 ( $\text{N}^9\text{H}$ ), 3084 ( $\text{NH}^{12}$ ), 1605 ( $\text{C}=\text{O}^{10}$ ), 1506 ( $\text{C}=\text{O}^{14}$ ), 1221 (N-N), 1508 (Ar-OCH<sub>3</sub>), 1221 (CH=CH), 456 (M-O), 424 (M-N); Molar conductance: 14.92  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ .

**(iii) [Cu(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O:**  $\text{C}_{34}\text{H}_{32}\text{Cl}_2\text{CuN}_6\text{O}_6.\text{H}_2\text{O}$ : Yield: 74%; Color: Dark green; M.p :290-292 °C; Mol.wt: 773.10; Elemental analyses: calculated and found (%): C: 54.08 (54.68), H: 4.27 (4.63), N: 11.13 (11.34); IR (KBr,  $\text{cm}^{-1}$ ): 3445 ( $\text{H}_2\text{O}$ ), 3196 ( $\text{NH}^9$ ), 3056 ( $\text{NH}^{12}$ ), 1592 ( $\text{C}=\text{O}^{10}$ ), 1504 ( $\text{C}=\text{O}^{14}$ ), 1219 (N-N), 1504 (Ar-OCH<sub>3</sub>), 1219 (CH=CH), 437 (M-O), 418 (M-N); Molar conductance: 57.40  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ .

**(iv) [Zn(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O:**  $\text{C}_{34}\text{H}_{32}\text{Cl}_2\text{N}_6\text{O}_6\text{Zn}$ : Yield: 66%; Color: White; M.p: 269-272 °C; Mol.wt: 756.97; Elemental analyses: calculated and found (%): C: 53.95 (54.15), H: 4.26 (4.42), N: 11.10 (11.58); IR (KBr,  $\text{cm}^{-1}$ ): 3228 ( $\text{NH}^9$ ), 3068 ( $\text{NH}^{12}$ ), 1594 ( $\text{C}=\text{O}^{10}$ ), 1542 ( $\text{C}=\text{O}^{14}$ ), 1218 (N-N), 1542 (A-OCH<sub>3</sub>), 1218 (CH=CH), 456 (M-O), 427 (M-N); Molar conductance: 54.92  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ .

**(v) [Mn(MPH)<sub>2</sub>Cl]Cl:**  $\text{C}_{34}\text{H}_{32}\text{Cl}_2\text{MnN}_6\text{O}_6$ : Yield: 71%; Color: light orange; M.p: 281-283 °C; Mol.wt: 746.49; Elemental analyses: calculated and found (%): C: 54.70 (55.10), H: 4.32 (4.72), N: 11.26 (11.48); IR (KBr,  $\text{cm}^{-1}$ ): 3181 ( $\text{NH}^9$ ), 3018 ( $\text{NH}^{12}$ ), 1598 ( $\text{C}=\text{O}^{10}$ ), 1511 ( $\text{C}=\text{O}^{14}$ ), 1242 (N-N), 1541 (A-OCH<sub>3</sub>), 1249 (CH=CH), 458 (M-O), 416 (M-N); Molar conductance: 58.62  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ .

## Biological studies

### Antioxidant activity:

The free radical scavenging activity of the ligand MPH and their complexes was measured *in-vitro* by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay. The stock solution was prepared by dissolving 24 mg of DPPH with 100 mL of methanol and stored at 20 °C until required. The working solution was obtained by diluting the DPPH solution with methanol to attain an absorbance of about 0.98±0.02 at 517 nm using a spectrophotometer. All the tested samples in various concentrations (50, 75 and 100 µg/mL) were prepared in methanol and the homogeneous solutions were achieved by stirring. An aliquot of test sample (1 mL) was added to 4 mL of 0.004% (w/v) methanolic solution of DPPH and then reaction mixture was vortexed for 1 min and kept at room temperature for 30 min in the dark to complete the reaction. The absorbance was read against blank at 517 nm. The synthetic antioxidant butylated hydroxytoluene (BHT) was used as the positive control (11). The ability of the tested samples at tested concentration to scavenge DPPH radicals was calculated using the equation below.

$$\text{Scavenging ratio (\%)} = [(A_i - A_o) / (A_c - A_o)] \times 100\%$$

Where  $A_i$  is the absorbance in the presence of the test compound;  $A_o$  is absorbance of the blank in the absence of the test compound and  $A_c$  is the absorbance in the absence of the test compound.

### Molecular docking studies

Molecular modeling studies were performed by using Hex 8.2 protein-ligand docking in PDB formats. The parameters used for docking include: correlation type-shape only, FFT mode 3D, grid dimension 0.6, receptor range 180, ligand range 180, twist range 360, distance range 40. The starting coordinates of the human antioxidant enzyme in complexes with the competitive inhibitor DTT (PDB: 3MNG) were taken from the Protein Data Bank (<http://www.rcsb.org/pdb>) (12-14). The ligand was docked against the lead competitive inhibitor ligand DTT at the crystal enzyme structure of the target protein and the best energy conformations of receptor ligand was studied and the binding energy was calculated

as the difference between the energy of the MPH, metal complexes and the individual energy of enzyme. In order to interrupt the binding interactions modes of the MPH and metal complexes with human antioxidant enzyme DTT (PDB: 3MNG).

### Physical measurements

Elemental analyses (C, H, N) were performed with a Perkin-Elmer 2400 series II analyzer. Molar conductance values ( $10^{-3} \text{mol/L}$ ) of the complexes in DMSO at 28 °C were measured using an EQUIP-TRONICS model-660A instrument. Melting point of the synthesized compounds was recorded by using apparatus model code NAMPA/045. UV-Visible spectra were measured in DMF/DMSO on an Ocean Optics USB 4000USA spectrophotometer, using 1 cm path length cuvette at room temperature. Infrared spectra were recorded using FT-IR 8400s Shimadzu spectrometer with KBr pellets in the range of 400-4000  $\text{cm}^{-1}$ . The NMR spectra have been recorded as 400 MHz Varian-AS NMR

spectrometer in DMSO- $d_6$  using tetramethylsilane (TMS) as the internal standard. Thermal measurements (TGA, DTA, 28–900 °C) were noted on a DTG-50 Shimadzu thermo-gravimetric analyzer at a heating rate of 10 °C/min and nitrogen flow rate of 20 mL/min. Magnetic susceptibilities were recorded with a Sherwood scientific magnetic susceptibility balance at 298 K. Mass spectra was recorded using the instrument Code; SC/AD/10-014.

## RESULTS AND DISCUSSION

The molar conductance of  $0.1 \times 10^{-2}$  mol/L solution in DMF was recorded; the synthesized 3d series metal complexes have been confirmed by physico-chemical techniques. The synthesized complexes such as  $[\text{Ni}(\text{LMPH})_2\text{Cl}_2]\text{H}_2\text{O}$ ,  $[\text{Co}(\text{LMPH})_2\text{Cl}_2]$ ,  $[\text{Cu}(\text{MPH})_2\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$ ,  $[\text{Zn}(\text{MPH})_2\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$  and  $[\text{Mn}(\text{MPH})_2\text{Cl}]\text{Cl}$  are quite stable in air and soluble in some organic solvents such as DMF and DMSO. The elemental analyses and molar conductivity values were in premising agreement with the suggested structure. The molar conductivity of  $[\text{Ni}(\text{LMPH})_2\text{Cl}_2]\text{H}_2\text{O}$  and  $[\text{Co}(\text{MPH})_2\text{Cl}_2]$  complexes were 15.72 and 14.92  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$  due to non electrolytic nature. Also, the molar conductances of  $[\text{Cu}(\text{MPH})_2\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$ ,  $[\text{Zn}(\text{MPH})_2\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$  and  $[\text{Mn}(\text{MPH})_2\text{Cl}]\text{Cl}$  were 57.40, 54.92 and 58.62  $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$  respectively due to uni-uni valent electrolytic state.

### $^1\text{H}$ NMR and Mass studies:

The proton NMR spectrum of ligand MPH showed at 8.24, 8.84 and 9.99 ppm (s, 3H,  $\text{NH}^{9, 12, 13}$ ) are assigned to NH protons of derivative of the semicarbazone group. The aromatic hydrogen resonance observed at 7.16 ppm (s, 1H, Ar- $\text{H}^2$ ), 6.56, 7.25 ppm (d, 2H, Ar- $\text{H}^4, 6$ ), 7.13 ppm (t, 1H, Ar- $\text{H}^5$ ), 3.71 ppm (s, 3H,  $\text{OCH}_3$ ). In addition, the doublets and triplets around 7.62, 7.61 ppm (d, 2H, Ar- $\text{H}^{19, 23}$ ) and 7.39-7.45 ppm (t, 3H, Ar- $\text{H}^{20, 21, 22}$ ) are due to aromatic ring protons were represented in Supplementary file S1. The mass spectrum confirms the formula of MPH by giving molecular ion peak ( $\text{M}^+$ ) corresponding to their molecular weight shown in Supplementary file S2.

### FT-IR Spectral studies:

Infrared spectrum of the ligand and their metal complexes were taken as KBr pellets. The strong bands appeared at 3182 ( $\text{NH}^9$ ), 3243 ( $\text{NH}^{12}$ ) and 3320 ( $\text{NH}^{13}$ )  $\text{cm}^{-1}$  assignable to  $\nu(\text{NH})$  of the derivative of semicarbazone group. One band

disappeared out of three in the IR spectra of metal complexes like  $[\text{Ni}(\text{MPH})_2\text{Cl}_2]\text{H}_2\text{O}$ ,  $[\text{Co}(\text{MPH})_2\text{Cl}_2]$ ,  $[\text{Cu}(\text{MPH})_2\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$ ,  $[\text{Zn}(\text{MPH})_2\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$  and  $[\text{Mn}(\text{MPH})_2\text{Cl}]\text{Cl}$  which showed the deprotonation of the NH group (12–13). The strong band observed at 1604  $\text{cm}^{-1}$  range in the uncoordinated ligand have been assigned to  $\nu(\text{N-N})$  stretching vibrations. On complexation, these bands were observed at 1488–1542  $\text{cm}^{-1}$  to lower intensity, thus representing the coordination of  $=\text{N-N}=\text{N}$  nitrogen to metal ion and appearance of a new bands indicated  $-\text{N}=\text{N}-$  bond formation (14). A sharp bands observed at 1709, 1665  $\text{cm}^{-1}$  in derivative of semicarbazone mainly due to  $\nu(\text{C}=\text{O})$  stretching frequency, a split band is an indicative of *cis* arrangement of both C=O groups. These bands are shifted to lower frequency side at 1605–1542  $\text{cm}^{-1}$  which indicates that carbonyl oxygen involves in the coordination with metal ion (15). In the spectra of complexes, the appearance new bands in the region at 437–458  $\text{cm}^{-1}$  and 416–427  $\text{cm}^{-1}$  showed stretching vibrations of (M-N) and (M-O) respectively.

### Electronic absorption spectra and magnetic moment:

Electronic spectrum of gray colored cobalt(II) complex showed three strong bands at 14,598, 16,393 and 16,949  $\text{cm}^{-1}$  due to the  $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{2g}(\text{F})(\nu_1)$ ,  $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{A}_{2g}(\text{F})(\nu_2)$  and  $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{1g}(\text{P})(\nu_3)$  transitions, respectively (16). The observed magnetic moment values 3.92 B.M, also support the complex to have octahedral geometry (17). The spectrum of dark brown colored nickel(II) complex showed bands at 14,705, 16,000 and 16,949  $\text{cm}^{-1}$  respectively. These bands can be attributed to the transitions  $^3\text{A}_{2g}(\text{F}) \rightarrow ^3\text{T}_{2g}(\text{F})(\nu_1)$ ,  $^3\text{A}_{2g}(\text{F}) \rightarrow ^3\text{T}_{1g}(\text{F})(\nu_2)$  and  $^3\text{A}_{2g}(\text{F}) \rightarrow ^3\text{T}_{1g}(\text{P})(\nu_3)$  respectively. Three bands exhibited by nickel complex with magnetic moment 2.86 B.M may be due to octahedral geometry. Copper(II) complex showed strong bands at 14,492 and 16,393  $\text{cm}^{-1}$ , which can be assigned to the transitions  $^2\text{B}_{1g} \rightarrow ^2\text{A}_{1g}(\text{d}_x^2 - \text{y}^2 \leftarrow \text{d}_z^2)(\nu_1)$  and  $^2\text{B}_{1g} \rightarrow ^2\text{E}_g(\text{d}_x^2 - \text{y}^2 \leftarrow \text{d}_{xyz})(\nu_1)$ . The two bands of dark green colored copper(II) complex showed the magnetic moment value 1.76 B.M evidence for square pyramidal. The manganese(II) complex exhibits a band with weak intensity at 10,309  $\text{cm}^{-1}$  and its magnetic moment value 5.95 BM, which can be attributed to  $^6\text{A}_{1g} \rightarrow ^4\text{T}_{1g}$  transition in a square pyramidal environment (18). The electronic spectra of the ligand and complexes are presented in Figure 1.

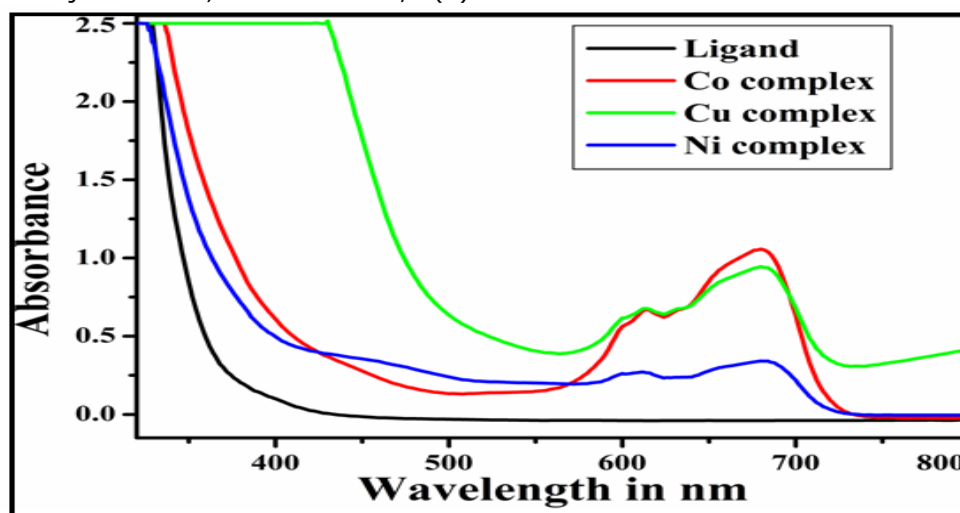


Figure 1: Electronic spectra of ligand and Ni(MPH)<sub>2</sub>Cl<sub>2</sub>]H<sub>2</sub>O, [Co(MPH)<sub>2</sub>Cl<sub>2</sub>] and [Cu(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O.

**Powder XRD analysis:**

Diffraction patterns of Ni(II), Co(II), Cu(II), Zn(II) and Mn(II) complexes have been carried out and recorded at 2θ = 10–80°, among them [Ni(MPH)<sub>2</sub>Cl<sub>2</sub>]H<sub>2</sub>O, [Cu(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O and

[Zn(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O complexes exhibited sharp peaks showed crystalline nature. The values of relative intensities, *d*, 2θ and sin2θ values of both observed and calculated are given in Tables 1 and 2.

**Table 1.** Diffraction pattern of [Cu(L)<sub>2</sub>Cl]Cl.H<sub>2</sub>O

Peak No	2θ (deg)	θ (deg)	Sinθ	Intensity (cps deg)	d (Å)		FWHM (deg)
					Calcd.	Obs.	
1	15.387	7.693	0.133	359.22	5.752	5.753	0.404
2	18.325	9.162	0.159	425.15	4.836	4.837	0.700
3	21.313	10.656	0.184	344.98	4.164	4.165	1.094
4	22.722	11.361	0.196	329.52	3.969	3.910	0.372
5	23.852	11.926	0.206	58.24	3.726	3.727	0.238
6	24.578	12.289	0.212	195.85	3.617	3.618	0.387
7	25.492	12.746	0.220	366.35	3.490	3.491	0.443
8	26.481	13.740	0.229	470.42	3.362	3.363	0.398
9	27.982	13.991	0.241	51.44	3.185	3.185	0.368
10	28.888	14.444	0.249	62.88	3.092	3.088	0.538

**Table 2.** Diffraction pattern of [Zn(L)<sub>2</sub>Cl]Cl.H<sub>2</sub>O

Peak No	2θ (deg)	θ (deg)	Sinθ	Intensity (cps deg)	d (Å)		FWHM (deg)
					Calcd.	Obs.	
1	16.362	8.184	0.142	144.34	5.411	5.413	0.561
2	20.268	10.134	0.176	10109.91	4.372	4.377	9.877
3	22.468	11.234	0.194	319.17	3.952	3.953	0.642
4	23.587	11.793	0.204	408.83	3.768	3.768	0.614
5	26.248	13.124	0.227	878.89	3.315	3.392	0.719
6	27.556	13.778	0.238	126.11	3.233	3.234	0.522
7	30.301	15.150	0.261	119.93	2.946	2.947	0.920
8	46.964	23.484	0.398	245.77	1.932	1.933	6.230

The diffraction patterns were further analyzed by using Debye Scherrer equation  $D = K\lambda/\beta\cos\theta$  Where *D* = size of the particle, *K* = dimensionless shape factor,  $\lambda$  = wavelength of the X-ray (1.5406 Å),  $\beta$  = full width half maximum  $\times 3.13/180$ ,  $\theta$  = Bragg’s diffraction angle, the metal complexes [Ni(MPH)<sub>2</sub>Cl<sub>2</sub>]H<sub>2</sub>O, [Cu(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O and [Zn(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O complexes are showing the nano-crystallinity size of 2.445, 11.225 and 20.275 nm respectively, while the other complexes exhibited amorphousness in nature (19). The

unit cell dimension can be calculated by using equation  $a = 2r\sqrt{2}$  for Cu(II) and Zn(II) complexes. Where *r* is the atomic radius of corresponding metals. For copper:  $a = 4.101\text{Å}$  and zinc:  $a = 3.931\text{Å}$ .

**Thermo gravimetric analysis of metal complexes:**

The thermogravimetric analysis was carried out in the temperature range 30–850 °C. Metal complexes of [Ni(MPH)<sub>2</sub>Cl<sub>2</sub>]H<sub>2</sub>O, [Cu(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O and [Zn(MPH)<sub>2</sub>Cl]Cl.H<sub>2</sub>O

showed mass loss of calculated: 2.34, 2.32 and 2.31% (found: 2.44, 2.48 and 2.58%) in the temperature range 99-170 °C, 90-160 °C and 99-180 °C, showed the dissociation of water molecules. The second stage of mass loss involves in the temperature range 180-240 °C, 170-220 °C and 180-240 °C, mass loss 9.24, 9.18 and 9.11% (9.11, 10.01 and 9.24%) assigned to dissociation of two chlorine atoms, the next stage involves the dissociation in the temperature range 260-380 °C, 220-310 °C and 240-380 °C respectively, with weight loss 27.62, 27.45 and 27.24% (2.44, 2.48 and 2.58%) which corresponds to the decomposition of methoxy benzene moiety (20-21). The fourth step at 380-600 °C, 310-580 °C and 380-630 °C respectively, with weight loss 51.07, 50.75 and 51.71% (50.01, 49.08 and 51.88%) the removal of phenyl group moiety and the metal residue of NiO, CuO and ZnO with weight loss of 9.72, 10.28 and 9.10% (10.06, 10.30 and 9.18%) from 610-850 °C. Also, the TGA curves of the [Co(MPH)<sub>2</sub>Cl<sub>2</sub>] and [Mn(MPH)<sub>2</sub>Cl]Cl showed three stages of degradation. The first stage from 180-240 °C and 180-230 °C with weight loss 9.46 and 9.51% (10.11 and 10.12%) was attributed to the loss of equivalent mass of two chlorine atoms, the second step with weight loss 28.28 and 28.39% (29.01 and

28.76%) from 220-305 °C and 240-330 °C corresponded to the removal of methoxy benzene moiety. In the third stage from 310-600 °C and 330-600 °C with weight loss 52.36 and 52.10% (51.66 and 50.88%) which involves in the removal of phenyl group moiety. The mass of the final residue, weight loss of 9.91 and 9.96% (10.22, and 10.17%) occur from 620-800 °C as stable metal residue of CoO and MnO. Degradation mechanism and kinetic and thermodynamic parameters of the synthesized complexes has been evaluated by Broido's graphical method for straight-line decomposition portion of the thermodynamic analytical curve (22). Energy of activation ( $E_a$ ) were calculated by the slope of  $\ln(\ln(1/y))$  versus  $1/T \times 10^{-3}$ . The thermodynamic properties like change in enthalpy ( $\Delta H$ ), entropy change ( $\Delta S$ ), free energy change ( $\Delta G$ ) and frequency factor ( $\ln A$ ) are calculated using the standard equations by employing Broido's relation:  $-\ln[\ln(1/y)] = E_a/RT_d - \ln A - \ln(8.314/T_d)$  where  $y$  is the fraction of the complex undecomposed,  $T_d$  is the decomposition temperature,  $R$  is the gas constant and  $E_a$  is the activation energy in kJ/mol. The nature of decomposition curve for metal complexes are represented in Figure 2.

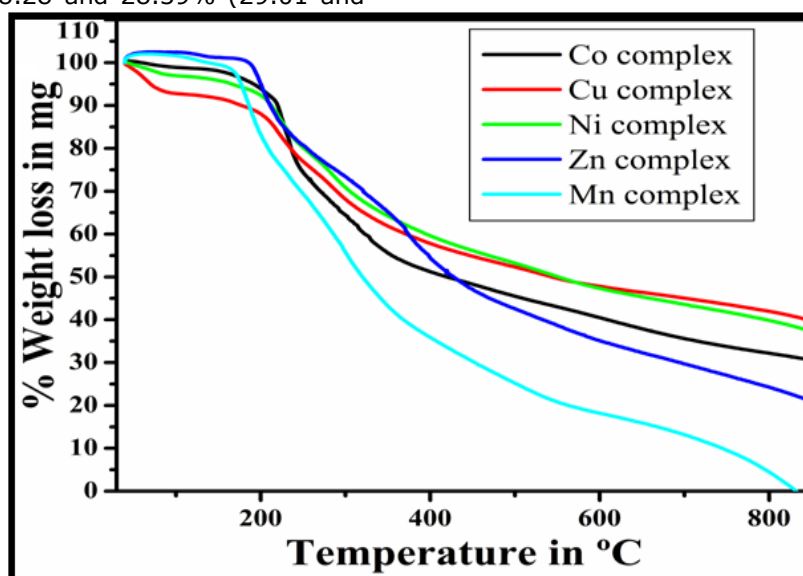


Figure 2: TGA curves of metal complexes.

The major weight loss for all the complexes was found in the temperature range 222.03-294.60 °C. The activation energies of zinc(II) complex (14.381 kJ/mol) and cobalt(II) complex (8.196 kJ/mol) were found to be very high, which accounts for their rapid degradation compared to nickel(II) complex (6.345 kJ/mol), manganese(II) complex (6.343 kJ/mol) and copper(II) complex (5.623 kJ/mol) that exhibit higher thermal stability was in the order of Zn > Mn > Co > Ni > Cu. The negative values of  $\Delta S$  indicated that the decomposition reactions are slower than normal. The positive sign of  $\Delta G$  values for the investigated complexes indicated that the free energy of the final residue was

higher than that of the initial compound and all the decomposition stages are non-isothermal processes. The major weight losses for all the complexes were found in the temperature range 222.03-294.60 °C. The activation energies of Zn(II) (14.381 kJ/mol) and Co(II) (8.196 kJ/mol) were found to be very high, which accounts for their rapid degradation compared to Ni(II) (6.345 kJ/mol), Mn(II) (6.343 kJ/mol) and Cu(II) (5.623 kJ/mol) that exhibit higher thermal stability was in the order of Zn > Co > Ni > Mn > Cu. The negative values of  $\Delta S$  indicated that the decomposition reactions are slower than normal. The positive sign of  $\Delta G$  values for the investigated complexes indicated

that the free energy of the final residue is higher than that of the initial compound and all the decomposition stages are non-isothermal processes.

**Biological evaluation**

**Antioxidant activity:**

The free radical scavenging ability of the synthesized ligand MPH and their metal complexes such as  $[\text{Ni}(\text{L})_2\text{Cl}_2]\text{H}_2\text{O}$ ,  $[\text{Co}(\text{L})_2\text{Cl}_2]$ ,  $[\text{Cu}(\text{L})_2\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$ ,  $[\text{Zn}(\text{L})_2\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$  and

$[\text{Mn}(\text{L})_2\text{Cl}]\text{Cl}$  were evaluated at different concentrations. The metal complexes found to be more potent antioxidant activity as compared to uncoordinated ligand. In which, the Co(II), Cu(II) and Zn(II) complexes assigning more antioxidant result approximately close to the standard butylated hydroxytoluene and Ni(II) and Mn(II) complexes exhibited moderate activity when compared with BHT. The activity is due the chelation of semicarbazone nucleus in the coordinated metal ion with the ligand (23). The results were shown Figure 3.

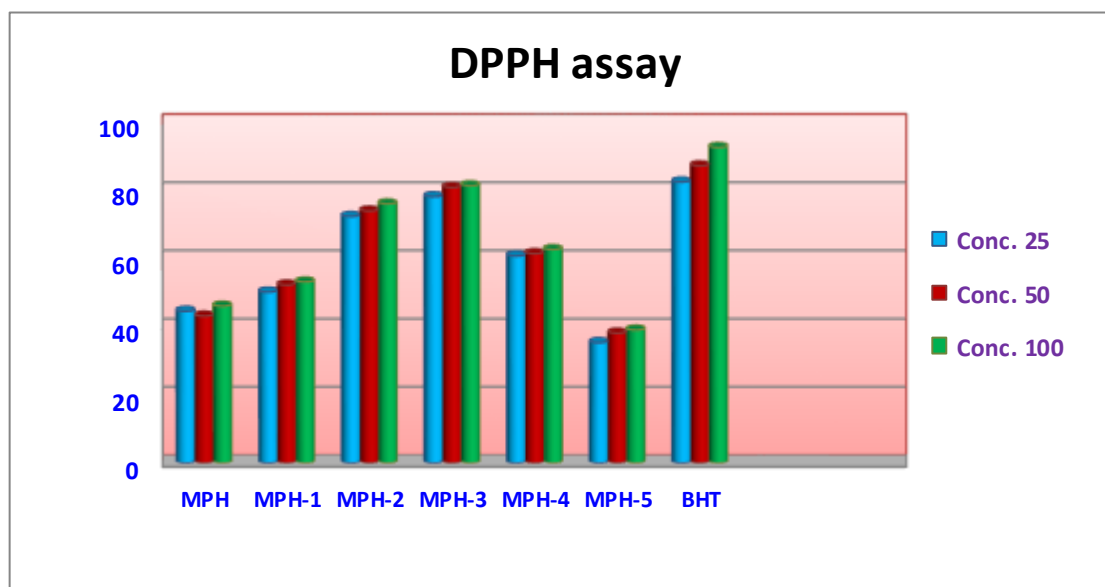


Figure 3: Antioxidant data of the ligand MPH and its metal complexes.

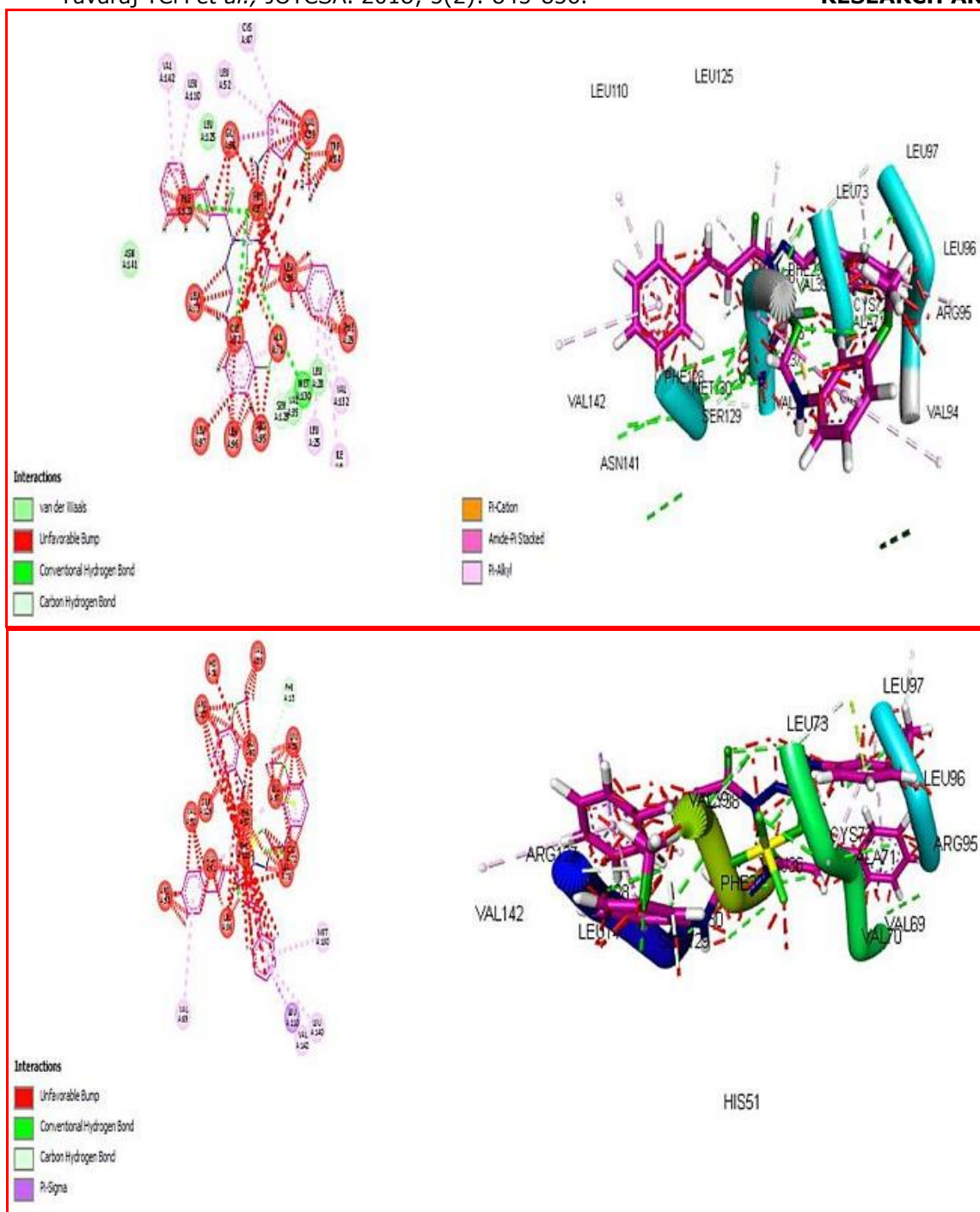
**Molecular docking studies:**

The docking studies of all the complexes showed prominent binding interactions, Co(II), Cu(II) and Zn(II) complexes offer the highest binding energy of -335.61, -329.54, -330.02 kcal/mol, while Ni(II) complex showed and -318.17 kcal/mol with human antioxidant 3MNG protein receptor by the key of amino acid residues are PHE128, LEU97, VAL39, LEU110, LEU125, GLY38, ARG127, HIS51, PHE37, GLY38, ARG127, HIS51, LEU36, VAL39, LEU125, LEU96, CYS72, LEU97, GLY38, ARG127, PHE37, MET130, LEU36, PHE29, ALA71, LEU97, VAL39, PRO40, LEU125, ARG127, and LEU36 (24). The

binding interaction of ligand with receptors amino acid residues shows conventional hydrogen bond, pi-alkyl and pi-sigma interaction bonds as shown in Figures 4 and 5. The interesting binding sites present in the receptor will favors the binding interaction with ligand, the computational docking studies were done for good docking scored complexes reveals that they showed good antioxidant inhibition activity (25-27). Finally, the results are good comparison for the wet analysis of antioxidant study. These results are shown in Table 3.

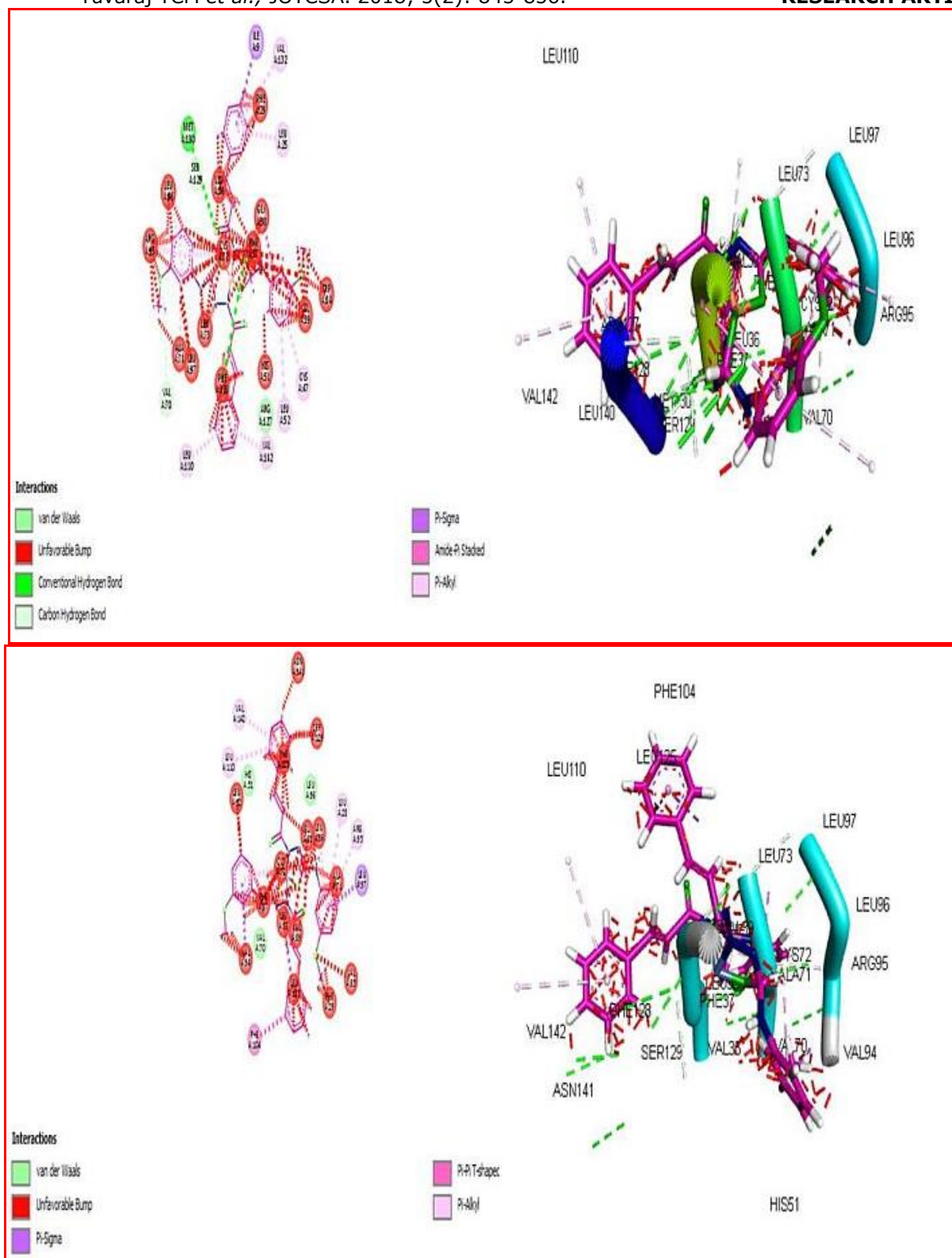
Table 3: Docking scores of metal complexes.

Compounds	Receptor PDB code	ΔG (kcal/mol)
MPH	3MNG	-240.51
$[\text{Ni}(\text{MPH})_2\text{Cl}_2]\text{H}_2\text{O}$	3MNG	-318.61
$[\text{Co}(\text{MPH})_2\text{Cl}_2]$	3MNG	-329.54
$[\text{Cu}(\text{MPH})_2\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$	3MNG	-330.02
$[\text{Zn}(\text{MPH})_2\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$	3MNG	-335.17



**Figure 4:** 3D & 2D binding interactions of  $[Ni(L)_2Cl_2] \cdot H_2O$  and  $[Co(L)_2Cl_2]$





**Figure 5:** 3D & 2D binding interactions of  $[Cu(L)_2Cl]Cl.H_2O$  and  $[Zn(L)_2Cl]Cl.H_2O$

**Antimicrobial activity:**

The antibacterial and antifungal activity of the ligand and its metal complexes was evaluated against *S.aureus*, *B.subtilis* and *E.coli* bacteria by the agar well diffusion method using nutrient agar medium at  $\pm 37\text{ }^\circ\text{C}$ , incubated for 24 hrs and potato dextrose agar (PDA) for fungal strains like *C. neoformans*, *C.albicans* and *A.niger* at  $\pm 25\text{ }^\circ\text{C}$ , incubated for 48 to 78 hours.

Compounds were basically dissolved in DMSO and about 100  $\mu\text{L}$  of this compound were filled to pre labelled wells using micropipette (28). DMSO used as negative control and chloramphenicol and fluconazole were used as standards (positive control) for bactericide and fungicide. All the synthesized complexes and the uncoordinated ligand showed inhibition property, among them Cu(II), Zn(II) and Mn(II)

complexes showed excellent activity when compared to standards and represented in Table 4. Our results showed that ligand MPH least activity against *S. aureus* with 03±0.3 mm zone of inhibition, but the complexes MPH<sub>2</sub>, MPH<sub>3</sub> and MPH<sub>4</sub> indicated highest activity against *S. aureus* with zone of inhibition 13±0.1 mm. *B. subtilis* showed highest susceptibility against MPH<sub>3</sub>, MPH<sub>4</sub> and MPH<sub>5</sub> with zone of inhibition 15±0.1 mm. the complexes MPH<sub>3</sub>, MPH<sub>4</sub> and MPH<sub>5</sub>

showed a significant antibacterial activity against *E. coli* with zone of inhibition 12±0.3 mm (29). In case of antifungal activity, the highest activity was observed in MPH<sub>2</sub> against *C. neoformans* with 10±0.6 mm zone of inhibition. *C. albicans* showed highest susceptibility against complexes MPH<sub>3</sub>, MPH<sub>4</sub> and MPH<sub>5</sub> with zone of inhibition 10±0.1 mm respectively. Also, the complex MPH<sub>2</sub> showed highest activity aligned *A. niger* with 11±0.3 mm zone of inhibition.

**Table 4:** Zone inhibition of antimicrobial data

Compounds	Antibacterial zone inhibition in mm (mean ± SD)			Antifungal zone inhibition in mm (mean ± SD)		
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>C. neoformans</i>	<i>C. albicans</i>	<i>A. niger</i>
	<b>Ligand</b>	03±0.3	05±0.2	05±0.7	04±0.4	03±0.1
<b>MPH<sub>1</sub></b>	06±0.3	-	07±0.3	08±0.2	-	06±0.3
<b>MPH<sub>2</sub></b>	14±0.2	12±0.4	10±0.2	10±0.6	09±0.2	11±0.3
<b>MPH<sub>3</sub></b>	13±0.1	15±0.1	12±0.3	08±0.4	10±0.1	10±0.3
<b>MPH<sub>4</sub></b>	13±0.1	15±0.1	12±0.3	08±0.4	10±0.1	10±0.3
<b>MPH<sub>5</sub></b>	13±0.1	15±0.1	12±0.3	08±0.4	10±0.1	10±0.3
<b>Chloramphenicol</b>	15±0.2	16±0.3	13±0.3	12±0.2	11±0.4	13±0.3
<b>Fluconazole</b>	-	-	-	12±0.2	10±0.1	12±0.3
<b>DMSO</b>	0	0	0	0	0	0

## CONCLUSION

In the present work, the ligand and a series of its metal complexes [Ni(MPH)<sub>2</sub>Cl<sub>2</sub>].H<sub>2</sub>O, [Co(MPH)<sub>2</sub>Cl<sub>2</sub>], [Cu(MPH)<sub>2</sub>Cl].Cl.H<sub>2</sub>O, [Zn(MPH)<sub>2</sub>Cl].Cl.H<sub>2</sub>O and [Mn(MPH)<sub>2</sub>Cl].Cl have been synthesized by a conventional method. The obtained compounds were analyzed by various spectroscopic techniques. Thermogravimetric analyses curve explains step by step degradation and the results are also supported the stability of metal complexes in the order of Zn(II) > Mn(II) > Co(II) > Ni(II) > Cu(II) complexes. The synthesized ligand is bidentate and coordinates through the nitrogen and carbonyl oxygen atoms of semicarbazone derivative. The two chlorine atoms also occupy the two sites of each metal giving an octahedral geometry for nickel(II) and cobalt(II) complexes. However, copper(II) complex is square pyramidal. The 2D and 3D binding interactions of all metal complexes exhibited highest binding energy scores as compared to ligand with human 3MNG protein receptor. In case of antioxidant activity, the cobalt(II), copper(II), and zinc(II) complexes showed better results than other complexes. The complexes were also screened for antimicrobial and molecular docking studies. The results are suggested that the complexes more prominent when compared to uncoordinated ligand, but

less prominent in comparison with standard drugs.

## ACKNOWLEDGEMENT

The authors thank Sahyadri Science College Shivamogga and Manipal Institute of Technology for providing analytical data analysis. Manipal, Karnataka, INDIA.

## REFERENCES

1. Asghar SF, Yasin KA, Habib-ur-Rehman, Aziz S. Synthesis and cyclisation of 1,4-disubstituted semicarbazides. Natural Product Research. 2010 Mar 10;24(4):315–25
2. Rajesh-Rane A, Shital-Naphade S, Pavan Kumar, Mahesh Palkar B, Mahamadhanif Shaikh S, Rajshekhkar Karpoomath. Synthesis of novel 4-nitropyrrole-based semicarbazide and thiosemicarbazide hybrids with antimicrobial and anti-tubercular activity. Bioorganic & Medicinal Chemistry Letters. 2014 Jul 24; 10: 3079-3083.
3. Pituchaa M, Karczmarzykb Z, Kosikowska U, and Malm A. Synthesis, Experimental and Theoretical Study on the Structure of Some Semicarbazides with Potential Antibacterial Activity. Zeitschrift für Naturforschung B. 2011 Apr 66;(5) 971-87

4. Rafat-Mohareb M. and Abeer Mohamed A. Uses of 1-Cyanoacetyl-4-Phenyl-3-Thiosemicarbazide in the Synthesis of Antimicrobial and Antifungal Heterocyclic Compounds. *International Research Journal of Pure & Applied Chemistry*. 2012 Jul 2(2): 2012 144-155,
5. Gursoy A, Terzioglu N, Otuk G. Synthesis of some new hydrazide-hydrazones, thiosemicarbazides and thiazolidinones as possible antimicrobials. *European Journal of Medicinal Chemistry*. 1997 Jun 32(9):753-757.
6. Narang KK, Singh VP. Synthesis and characterization of cobalt (II), nickel (II), copper (II) and zinc (II) complexes with acetylacetone bis-benzoyl hydrazone and acetylacetone bis isonicotinoyl hydrazone. *Transition Metal Chemistry*. 1993 Dec 10(18): 287-290.
7. El-Azab AS, El-Tahir KEH. Synthesis and anticonvulsant evaluation of some new 2,3,8-trisubstituted-4(3H)-quinazoline derivatives. *Bioorganic & Medicinal Chemistry Letters*, 2012 Oct 22(1): 327-333.
8. Aly MM, Mohamed YA, El-Bayouki KAM, Basyouni WM, Abbas SY. Synthesis of some new 4(3H)-quinazolinone-2-carboxaldehyde thiosemicarbazones and their metal complexes and a study on their anticonvulsant, analgesic, cytotoxic and antimicrobial activities. *European Journal of Medicinal Chemistry*, 2010 Apr 45(8): 3365- 3373.
9. Azam F, Alkskas IA, Khokra SL, Prakash O. Synthesis of some novel N 4 - (naphtha[1,2-d]thiazol-2-yl) semicarbazides as potential anticonvulsants. *European Journal of Medicinal Chemistry*. 2009 Nov 44(1): 203-211.
10. Shashikumar ND, Krishnamurthy G, Bhojya-Naik HS, Lokesh MR, Jithendra-kumara KS. Synthesis of new biphenyl-substituted quinoline derivatives, preliminary screening and docking studies. *Journal of chemical sciences*. 2014 Jan 126(1): 205-212.
11. Manjuraj T, Krishnamurthy G, Yadav D. Bodke, BhojyaNaik H.S, Metal complexes of quinolin-8-yl [(5-methoxy-1H-benzimidazol-2-yl)sulfanyl]acetate: Spectral, XRD, thermal, cytotoxic, molecular docking and biological evaluation. *Journal of Molecular Structure*, Volume 1148, (15): 2017; 231-237.
12. Nakamoto K, *Infrared and Raman Spectra of Inorganic and Coordination Compounds*. In:Chalmers JM, Griffiths PR, editors. *Handbook of vibrational spectroscopy*, Chichester, UK: John Wiley & Sons, Ltd; 2006.
13. Sangeetha Gowda KR, Bhojya-Naik HS, Vinay-Kumar B, Sudhamani CN, Sudeep HV, Ravikumar-Naik TR, Krishnamurthy G. Synthesis, antimicrobial, DNA-binding and photonuclease studies of Cobalt(III) and Nickel(II) Schiff base complexes. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2013 Jun 105(10): 229-237.
14. Emelda AR, Jayachandramani N, Ravichandran S. Synthesis, Characterization and Antimicrobial Study of a New Mannich Base, N-(1-Piperidinobenzyl)benzamide and its Transition Metal(II) Complexes. *Asian Journal of Chemistry*. 2008 Feb 2(20): 2485-2490.
15. Ashraf A, Siddiqui WA, Akbar J, Mustafa G, Krautscheid H, Ullah N. Metal complexes of benzimidazole derived sulfonamide: Synthesis, molecular structures and antimicrobial activity. *Inorganic Chimca Acta*. 2016 Mar (443): 179-85.
16. Lever A.B.P. *Inorganic electronic spectroscopy*. 2nd ed. Amsterdam ; New York: Elsevier; 1984 863.
17. El-Gammal OA, Mostafa MM. Synthesis, characterization, molecular modeling and antioxidant activity of Girard's T thiosemicarbazide and its complexes with some transition metal ions *SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy*,2014 Mar(127): 530-42.
18. Rahaman F, Mruthyunjayaswamy BHM. Synthesis, spectral characterization and biological activity studies of transition metal complexes of Schiff base ligand containing indole moiety. *Complex Metals*. (31): (2014); 88-95.
19. Bal M, CEYHAN G, AVAR B, KÖSE M, Kayraldiz A, KURTOĞLU M. Synthesis and X-ray powder diffraction, electrochemical, and genotoxic properties of a new azo-Schiff base and its metal complexes. *Turkish journal of chemistry*. 2014 Apr 17;38(2):222-41.
20. Joseph J, Mehta HB. Synthesis, characterization, and thermal analysis of transition metal complexes of polydentate ONO donor Schiff base ligand. *Russian Journal of Coordination Chemistry*. 2007 Mar 12(33): 124-129.
21. Donia A. M, Al-Ansi T. Y and Othman M. Q., *Journal of Thermal Analysis*. (50) 1997 857.
22. Venugopala Reddy KR, Keshavayya J, Seetharamappa J. Synthesis, spectral, magnetic and thermal studies on symmetrically substituted metal (II) 1,3,8,10,15,17,22,24-octachloro phthalocyanines, *Dyes Pigments*, 2003 Nov (59):237-244.
23. Yapati H, Devineni S.R, Chirumamilla S, Kalluru S. Synthesis, characterization and studies on antioxidant and molecular docking of metal complexes of 1-(benzo[d]thiazol-2-

- Yuvaraj TCM *et al.*, JOTCSA. 2018; 5(2): 845-856.
- yl)thiourea. Journal of Chemical Sciences. 2016 Jan (128): 43-51.
24. Harinath Y, Subbarao D, Suresh C, Seshaiiah K. Synthesis, characterization and studies on antioxidant and molecular docking of metal complexes of 1-(benzo[d]thiazol-2-yl)thiourea. Journal of Chemical Sciences. 2016 Jan 128(1): 43-51.
25. Hall Parsonage D, Poole LB, Karplus PA. Structural evidence that peroxiredoxin catalytic power is based on transition-state stabilization. Journal of Molecular Biology. 2010 10; 402(1)194-209.
26. Abdel Nasser MA, Alaghaz-Badr A, El-Sayed A, Ahmed, El-Henawy, Reda, Ammar AA. Synthesis, spectroscopic characterization, potentiometric studies, cytotoxic studies and molecular docking studies of DNA binding of transition metal complexes with 1,1-diaminopropane-Schiff base. Journal of Molecular Structure, 2013 Dec 1035(12): 83-93.
- RESEARCH ARTICLE**
27. Mohammed Shafeeulla R, Ganganaiik Krishnamurthy, Halehatti S. Bhojynaik, Manjuraj T. Synthesis, Cytotoxicity, and Molecular Docking Study of Complexes Containing Thiazole Moiety. JOTCSA. 2017 Aug 4(3): 787-810.
28. Bhimagouda-Patil S, Krishnamurthy G, Bhojya-Naik HS, Prashant R. Latthe, Manjunath-Ghate. Synthesis, characterization and antimicrobial studies of 2-(4-methoxy-phenyl)-5-methyl-4-(2-arylsulfanyl-ethyl)-2,4-dihydro-[1,2,4] triazolo-3-ones and their corresponding sulfones. European Journal of Medicinal Chemistry 12(45): 3329-3334.
29. Jayamani A, Sengottuvelan N, Chakkaravarthi G, Synthesis, structural, electrochemical, DNA interaction, antimicrobial and molecular docking studies on dimeric copper(II) complexes involving some potential bidentate ligands. Polyhedron 2014 Feb 81(12): 764-76.