



## **Synthesis, Characterization and Antimicrobial studies of Schiff base Ligand from amino acid L-arginine and its Cu(II), Ni(II),Co(II) complexes**

Sree Devi R.K.<sup>1\*</sup>, S. SudhaKumari<sup>2</sup>

<sup>1\*</sup>Research scholar, Reg. No: 11775, Department of Chemistry, S.T. Hindu college, Nagercoil-629 002(Tamil Nadu) India. Affiliated to Manonmaniam Sundaranar University, Abishekapatti, Tirunelveli- 627 012, Tamil Nadu, India.

<sup>2</sup>Assistant Professor, Department of Chemistry, S.T. Hindu College, Nagercoil-629 002 (Tamil nadu) India.

**Abstract :** Transition metal complexes of Cu(II), Ni(II), Co(II) with a Schiff base Ligand (R,Z)-2-(2-hydroxy-3-methoxybenzylideneamino)-5-guanidinopentanoic acid (HMA-GPA) was synthesized by the condensation of 2-hydroxy-3-methoxybenzaldehyde and L- Arginine. These were characterized by elemental analysis IR, UV, magnetic susceptibility and molar conductivity measurements. The IR spectra of the Ligand HMA-GPA and the metal complexes suggest that the Ligand coordinates the metal ion through azomethine nitrogen, carboxylate Oxygen and Oxygen of the phenolic -OH group. The electronic absorption spectra and magnetic data indicate the Cu(II), Ni(II) complexes to be square planar and Co(II) complex to be octahedral. The metal complexes and the ligand were subjected to antimicrobial studies by Kirby Bayer Disc-diffusion method and found to have significant activity against the selected bacterial and fungal strains under study.

**Keywords :** 2-hydroxy-3-methoxy benzaldehyde, L-arginine, molar conductivity, antibacterial, antifungal activity.

### **Introduction**

The compounds having azomethine group (-CH=N-) are called Schiff bases. Schiff base Ligands form stable complexes with transition metal ions which have some importance in human physiological system<sup>1</sup>. Amino acids are mainly responsible for various process carrying out in daily routine inside all the living systems<sup>2</sup>. Schiff bases having carboxylic acid as part of their ligand especially with N,O donors can coordinate with the metal ion as monodentate, bidentate chelate or bridging manner<sup>3,4,5</sup>. Schiff base metal complexes exhibits pharmacologically significant antibacterial, antiulcer and analgesic activities<sup>6</sup>. The amino acid L-arginine

has significant role in cell division and immune functioning and has numerous biological applications<sup>7</sup>. Many research reviews have highlighted the antimicrobial activity of Schiff bases of arginine with various aldehydes<sup>8,9</sup>. Taking the above facts into consideration the synthesis of Schiff base Ligand HMA-GPA and its metal complexes Cu(II), Ni(II), Co(II) their characterization and their antimicrobial activity are discussed.

## Experimental

All the chemicals and the metal salts used were chemically pure grade. Elemental analysis were done with the help of Elementar Vario EL III. All these analysis were carried out at STIC, CUSAT Cochin. The IR spectra were recorded using Thermo Nicolet, Avatar 370 of range 4000-400  $\text{cm}^{-1}$ . UV-Visible spectra were obtained using Varian, Cary 5000 spectrophotometer in the range of 200-800 nm. Molar conductivity measurements were recorded by CM-82T Elico conductivity bridge in DMSO solvent. The magnetic moment values of the complexes were found using Guoy balance. Antimicrobial organisms were purchased Microbial Type Culture Collection and Gene Bank (MTCC) Chandigarh and tested using Disc diffusion method<sup>10</sup> carried out at Inbiotics, Institute of Biology and Clinical Research, Nagercoil, India. The bacterial strains were maintained on Nutrient Agar (NA).

### Synthesis of Schiff base Ligand (HMA-GPA)

The Schiff base Ligand (HMA-GPA) was synthesized by mixing of 20 ml 0.304 g ethanolic solution of 2-hydroxy-3-methoxy benzaldehyde (0.1 mol) and 20 ml 0.348 g aqueous solution of L- Arginine (0.1 mol) in 1:1 molar ratio. The resulting reaction mixture was refluxed with simultaneous stirring and heating for 4 hours at a temperature 65 °C and completion of the reaction can be tested by TLC. Then the solution was reduced to half of its initial volume by heating in a magnetic stirrer for one hour at a temperature of 65 °C and kept overnight without any disturbance. On mild heating yellowish flakes were separated out and they were filtered and washed several times with diethyl ether, then dried and stored over fused calcium chloride in a dessicator.

### Synthesis of Schiff base metal (II) complexes

To the 20 ml hot ethanolic solution of Schiff base ligand (HMA-GPA) (0.1 mol) was added a aqueous solution of 20 ml (0.1 mol)  $\text{Cu}(\text{NO}_3)_2 \cdot 3 \text{H}_2\text{O}$ ,  $\text{Ni}(\text{NO}_3)_2 \cdot 6 \text{H}_2\text{O}$  and  $\text{Co}(\text{NO}_3)_2 \cdot 6 \text{H}_2\text{O}$  separately drop by drop with continuous stirring in the Ligand: metal ratio 1:1. The clean solution was heated with a magnetic stirrer for 3 hrs 65 °C. Then 5-6 drops of 0.1 mol NaOH was added to the reaction mixture till a precipitate was obtained and the solution was heated for one hour. The resulting precipitate was filtered, washed many times by diethyl ether and finally dried in a vacuum and stored over anhydrous calcium chloride in a dessicator.

## Results and Discussion

### Elemental analysis

The elemental analysis of the Schiff base Ligand (HMA-GPA) and the metal complexes Cu(II), Ni(II) and Co(II) shown in table .1 were in well agreement with the proposed chemical formula and indicates 1:1 stoichiometry for metal:ligand ratio.

**Table.1 Analytical data of the Schiff base Ligand (HMA-GPA) and metal (II) complexes**

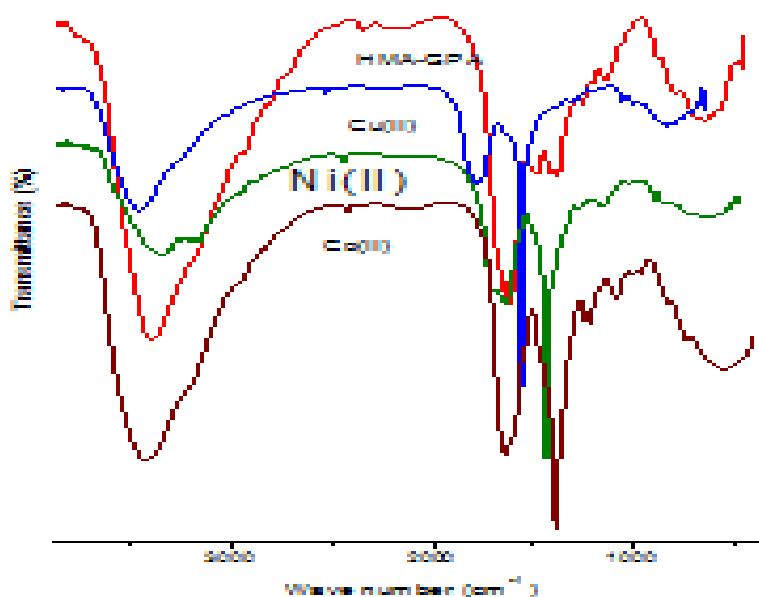
Compound	colour	Yield %	Mol. Wt.	Elemental analysis(%)(calcd.)/(found)			
				C	H	N	M
HMA-GPA	Dark Yellow	70	308	54.54 (54.11)	6.54 (6.20)	18.17 (17.96)	--
Cu(II)complex	Blackish green	65	584	28.80 (28.56)	4.83 (4.72)	14.39 14.10	10.88 (10.20)
Ni(II) complex	Brown	68	525	32.03 (31.93)	4.22 (4.05)	16.01 (15.91)	11.18 (11.12)
Co(II) complex	Brown	69	579	29.02 (29.46)	4.87 (4.93)	14.51 (14.67)	10.17 (10.92)

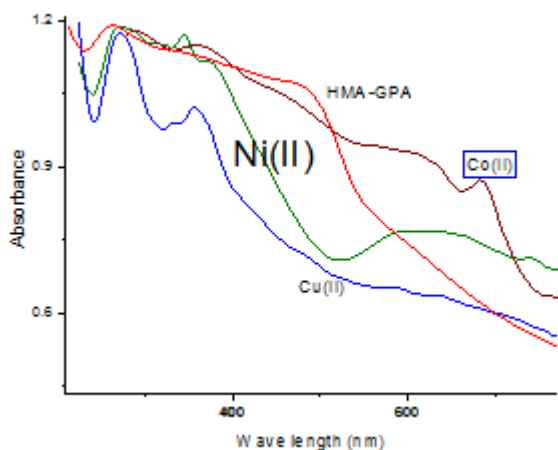
**Table.2 Characteristic IR bands of Ligand (HMA-GPA) and metal (II) complexes in  $\text{cm}^{-1}$** 

Compound	$\nu_{\text{OH}}$ (phenolic/ $\text{H}_2\text{O}$ )	$\nu$ (CH=N)	$\nu_{\text{COO}^-}$ asy	$\nu_{\text{COO}^-}$ sym	$\nu$ (C-O)	$\nu$ (M-O)	$\nu$ (M-N)	Others
HMA-GPA	3429	1638	1599	1350	1231	--	--	
Cu(II) complex	3446 838	1628	1587	1364	1224	603	461	1383 ( $\text{NO}_3^-$ )
Ni(II) complex	3380 829	1626	1589	1360	1219	555	485	1384 ( $\text{NO}_3^-$ )
Co(II) complex	3432 833	1630	1585	1365	1208	550	484	1384

### IR Spectra

The IR spectra of the Ligand (HMA-GPA) and the Cu(II), Ni(II) and Co(II) metal complexes were shown in the **fig. 1**. IR spectra of HMA-GPA exhibit bands of azomethine linkage  $\nu$  (-CH=N-) at  $1638 \text{ cm}^{-1}$ , Phenolic  $\nu$  (C-O) stretching at  $1231 \text{ cm}^{-1}$  and intense bands of asymmetric stretching  $\nu_{\text{asy}}(\text{COO}^-)$  at  $1599 \text{ cm}^{-1}$ , symmetric stretching vibration  $\nu_{\text{sym}}(\text{COO}^-)$  at  $1350 \text{ cm}^{-1}$  of carboxylate moiety. The broad band found in the region  $3429 \text{ cm}^{-1}$  may be due to the  $\nu$  (-OH) stretching vibration. In Cu(II), Ni(II) and Co(II) metal complexes all these bands were shifted to lower wave numbers  $1626\text{-}1630 \text{ cm}^{-1}$  of  $\nu$  (-CH=N-) confirms the coordination of azomethine group with the metal ions <sup>11</sup> and  $1208\text{-}1224 \text{ cm}^{-1}$  of phenolic  $\nu$  (C-O) stretching vibration underwent coordination with the metal ions after deprotonation. The asymmetric bands  $\nu_{\text{asy}}(\text{COO}^-)$  of carboxylate group found in the complex spectrum were shifted to lower frequencies  $1585\text{-}1589 \text{ cm}^{-1}$  and symmetric bands  $\nu_{\text{sym}}(\text{COO}^-)$  to higher frequencies from  $1360\text{-}1365 \text{ cm}^{-1}$  after the complexation process <sup>12</sup> and their magnitude difference between the stretching vibrations in the range  $220\text{-}229 \text{ cm}^{-1}$  indicates monodentate mode of coordination of carboxylate oxygen with the metal ion. A broad band found in all the metal complexes from  $3380\text{-}3446 \text{ cm}^{-1}$  can be assigned to the stretching frequency  $\nu$  (-OH) indicating the presence of water molecules. A sharp band observed at  $1383\text{-}1384 \text{ cm}^{-1}$  in all the three metal complexes were due to the uncoordinated nitrate ion <sup>13</sup> and this is confirmed by the presence of new  $\nu$  (M-O) and  $\nu$  (M-N) bands at  $550\text{-}603 \text{ cm}^{-1}$  and  $461\text{-}485 \text{ cm}^{-1}$  respectively.

**Fig.1. IR Spectra of Schiff base (HMA-GPA) and Cu(II), Ni(II), Co(II) complexes**



**Fig.2. UV Spectra of Schiff base (HMA-GPA) and Cu(II), Ni(II) , Co(II) complexes**

### UV Spectra

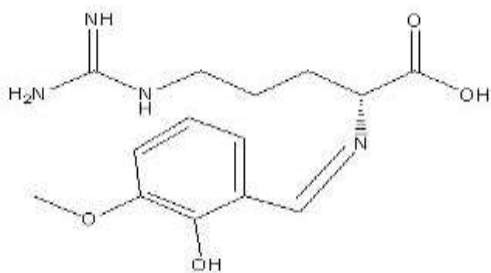
The electronic spectra of Cu(II) , Ni(II) and Co(II) metal complexes were recorded in DMSO at room temperature were shown in the **Fig. 2** The ligand displays two energy bands in the UV region at  $36764\text{ cm}^{-1}$  corresponding to  $\pi-\pi^*$  and  $28818\text{ cm}^{-1}$  corresponding to  $n-\pi^*$  transitions. In the spectra of Cu(II) complex, the absorption in the region  $17094\text{ cm}^{-1}$  and  $15797\text{ cm}^{-1}$  denotes a four coordinate square planar geometry<sup>14</sup> and the  ${}^2B_{1g} \rightarrow {}^2A_{1g}$ ,  ${}^2B_{1g} \rightarrow {}^2E_g$  transitions can be assigned<sup>15</sup>. The electronic spectra of Ni(II) complex exhibits band at  $16077\text{ cm}^{-1}$  which can be assigned to d-d transition  ${}^1A_{1g} \rightarrow {}^1A_{2g}$  and  $26881\text{ cm}^{-1}$  due to charge transfer. This indicates the square planar geometry of the complex<sup>16</sup>. The electronic spectra of Co(II) complex has its absorption bands in the region at  $19880\text{ cm}^{-1}$  and  $14388\text{ cm}^{-1}$  -  $12468\text{ cm}^{-1}$  with spin allowed transitions  ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$  and  ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$  respectively<sup>17</sup>.

### Magnetic susceptibility

The magnetic moments of Metal (II) complexes were calculated using the Guoy balance. The magnetic moment calculated for Cu(II) complex as 1.83 BM suggests that the complex is square planar and paramagnetic<sup>18</sup>. The diamagnetism behavior in the Ni(II) complex also confirms the square planar structure<sup>19</sup>. The calculated magnetic susceptibility measurements of the cobalt(II) complex is 4.93 suggests the six coordinated octahedral geometry<sup>20</sup>.

### Molar conductance Measurements

The observed molar conductance values are  $109, 107$  and  $94\text{ ohm}^{-1}\text{ cm}^2\text{ mol}^{-1}$  at concentration  $10^{-3}\text{ M}$  with DMSO solvent for Cu (II), Ni(II) and Co(II) complexes respectively. These high values are due to the displacement of  $\text{NO}_3^-$  ions by DMSO and suggest that the metal (II) complexes are electrolytes.



**Fig.3. Proposed structure of Schiff base Ligand ( HMA-GPA)**

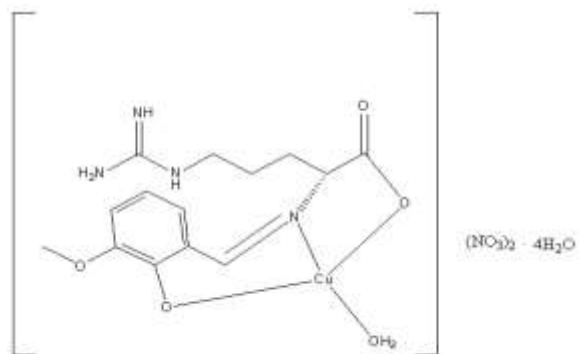


Fig. 4. Proposed structure of Cu(II) complex

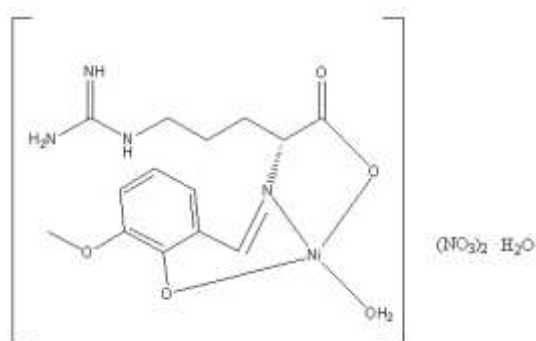


Fig. 5. Proposed structure of Ni (II) complex

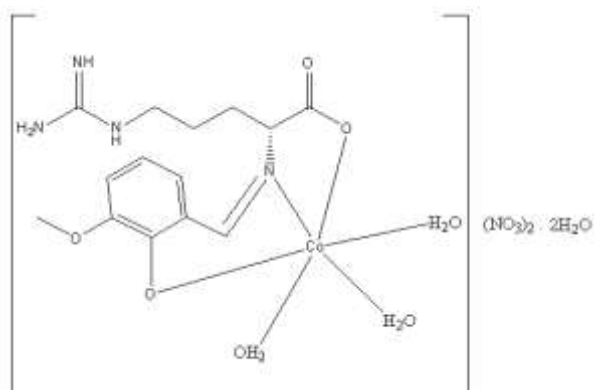


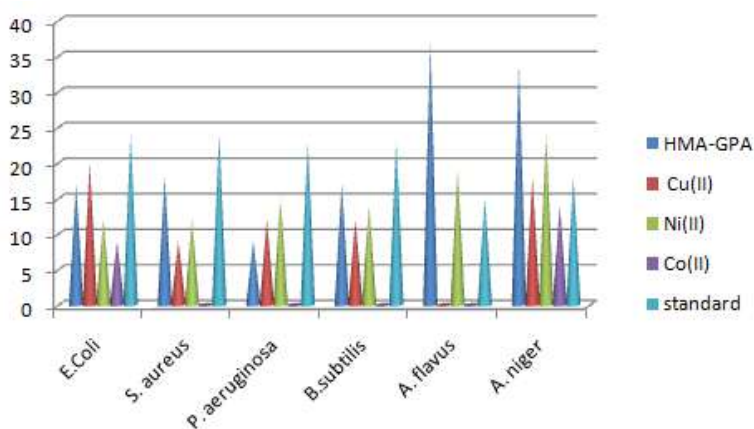
Fig.6 Proposed structure of Co(II) complex

Table 3. Antimicrobial activity of Schiff base HMA-GPA and Cu(II), Ni(II) complexes

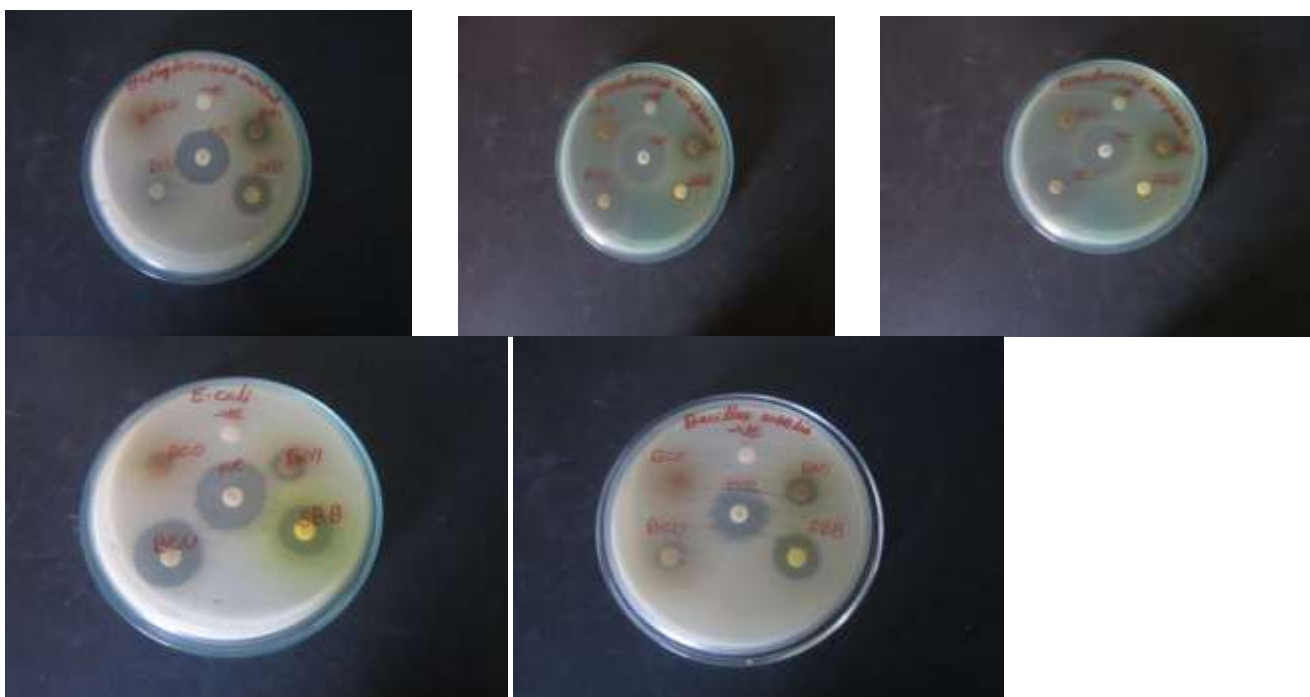
Compounds	Zone of inhibition (mm)					
	Bacteria				Fungi	
	E.Coli	S. aureus	P. aeruginosa	B. subtilis	A. niger	A. flavus
HMA-GPA	17	18	9	17	34	37
Cu(II)	20	9	12	12	18	--
Ni(II)	12	12	15	14	24	19
Co(II)	9	--	--	--	14	--
Streptomycin	24	24	23	23	--	--
Flucanazole	--	--	--	--	18	15

## Antimicrobial activity

The antimicrobial activities of Schiff base ligand HMA-GPA and its metal complexes have been determined against four bacterial strains *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and two fungal strains *Aspergillus niger* and *Aspergillus flavus* at a concentration of sample 0.1 mg/1ml in DMSO using Disc-diffusion method and the results are shown in the table 3. Streptomycin is used as positive control for bacteria and Flucanazole as positive control for Fungal species. Ligand exhibits better activity in case of *S. aureus* and *B. subtilis*. Cu(II) and Ni(II) complexes show more activity than their parent ligand in case of *P. aeruginosa*. Cu(II) complex shows good activity against *E. coli*. Co(II) complex exhibited small activity against *E. coli* but failed to show any activity against any of the bacterial species. The ligand and the metal complexes show more significant antifungal activities against *A. niger* than their standard and less pronounced antibacterial activities (Fig.7 & 8). The increased inhibition activities can be explained on the basis of Overton's concept<sup>21</sup> and Chelation theory<sup>22</sup>. The normal cell process can also be disturbed by the formation of hydrogen bond through the azomethine nitrogen with the active centers of cell constituents. The differences in the activity of ligand and their metal complexes against microorganisms can be attributed to the variation in the ribosomes of microbial cells and the impermeability of the cells<sup>23</sup>.



**Fig.7** Graphical representation of Antimicrobial activity of HMA-GPA ligand and Cu(II), Ni(II) complexes





**Fig. 8. Antibacterial and Antifungal activity of Ligand HMA-GPA and metal (II) complexes**

## References

1. Sanyan L. A, Ankel, Kirishnamurti C., Comparative cytotoxic and biochemical effects of ligands and metal complexes of alpha-N-heterocyclic carboxaldehyde thiosemicarbazones, *J Med Chem.*, 1979, 22(10), 1218-1221.
2. Vassilev K, Dimitrova M, Turmanova S, Milina R., Catalytic activity of histidine metal complexes in oxidation reactions, *Syn React Inorg Met.*, 2013, 43, 243-249.
3. Garnovskii A.D, Nivorozhkin A.L, Minkin V.I., Hom- and heteroatomic chalcogen rings, *Coord. Chem. Rev.*, 2003, 126, 1-69.
4. Badwaik V.B, Deshmukh R.D, Aswar A.S., Transition metal complexes of a Schiffbase: synthesis, characterization, and antibacterial studies, *J. Coord. Chem.*, 2009, 62, 2037-2047.
5. Hosny N.M, Sherif Y.E, El-Rahman A.A., Spectral characterization and anti-inflammatory activity of Schiff-base complexes derived from leucine and 2-acetylpyridine, *J. Coord. Chem.*, 2008, 61, 2536-2548.
6. Mehmet G, Mehmet S, Ismet B., Synthesis, characterization and antimicrobial activity of a new pyrimidine Schiff base and its Cu(II), Ni(II), Co(II), Pt(II) and Pd(II) complexes, *Turk J Chem.*, 2012, 36, 189-200
7. Webpage <https://aminoacidsguide.com/Thr.html> [Accessed June 21, 2018]
8. Sakiyan I, Ozdemir R, Ogutcu H., Synthesis Characterization and Antimicrobial Activities of New N-(2-hydroxy-1-naphthalidene)-amino Acid (L-Tyrosine, L-Arginine and L-lysine) Schiff Bases and their Manganese (III) complexes, *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry.*, 2014, 44, 417-423.
9. Iniama, Grace E, Iorkpiligh, Terungwa Isaac., Synthesis, Characterization and Antimicrobial Studies of Mn(II) Co(II) and Zn(II) Schiff Base Complexes Derived from L-Arginine and 2-Hydroxy-1-Naphthaldehyde, *International Journal of science and Research (IJSR).*, 2013, 2319-7064.
10. Bauer A.W, Kirby W.N, Sheries J.C, Turck M., Antibiotic susceptibility testing by a standardized single disc method, *Am Jour. clin. Pathol.*, 1966, 45(4), 493 - 496.
11. Azza Abu-Hussen, Adel Emara., Metal complexes of some thiocarbohydrazone ligands: synthesis and structure, *J. Coord. Chem.*, 2004, 57(11), 973.
12. Gamo I., Infrared Spectra of Water of Crystallization in some Inorganic Chlorides and Sulfate, *Bull. Chem. Soc.*, 1961, 34, 760-764.
13. Mariana L.D, Angela K, Nicoale S, Adin M.M., Transition metal M(II) complexes with isonicotinic acid 2-(9-anthrylmethylene)-hydrazide, *J. Serb. Chem. Soc.*, 2010, 75(11), 1515-1531.
14. Bjerrum J, Ball Hausen C.J, Jorgensen C.K., Studies on Absorption Spectra: Results of Calculations on the spectra and configuration of Copper(II) ions, *Stereochemistry of ionic Solids.*, *Acta Chem. Scand.*, 1954, 8, 1275.
15. Parmar N.J, Teraiya S.B., Cobalt(II) and nickel(II) chelates of some 5-pyrazolone-based, Schiff-base ligands, *J. Coord. Chem.*, 2009, 62(14), 2388-2398.
16. R. Dingle, The Electronic Spectrum of Crystalline Bis (diethyldithiocarbamate) nickel (II), *Inorganic Chemistry.*, 1968, 10(6), 1141.
17. Robert C, Rosenberg, Root C.A, Gray H.B., Electronic spectral and magnetic susceptibility studies of nickel(II), cobalt(II) carboxy peptides A complexes, *J. Am. Chem. Soc.*, 1975, 97, 21-26.

18. B.N. Figgs and J. Lewis.,Progress in Inorganic Chemistry, edited by F.A. Cotton InterScience, New York,1964, vol.6, 37.
19. Raman N, Raja S.J, Joseph J, Sakthivel A.,Designing, structural elucidation, comparison of DNA cleavage and antibacterial activity of metal(II) complexes containing tetradentate Schiff base,Russ. J. Coord. Chem., 2008,34, 842.
20. Figgs B.N., Introduction to Ligand Field., Wiley, New York, NY,USA, 1966.
21. Anjaneyula Y, Rao R.P., Preparation, characterization and antimicrobial activity studies on some Ternary complexes of Cu(II) with Acetyl acetone and various salicylic acids, Synth react inorg. met-org Chem., 26,257(1986).
22. Mishra, Lallan Singh, Vinodh Kumar, Synthesis, Structural and antifungal studies of Co(II), Ni(II) and Cu(II) and Zn(II) complexes with new Schiff bases bearing benzimidazoles, Indian JChem,1993,32A(05).
23. Raman N, Kulandaisamy A, Shunmugasundaram A,Jeyasubramanian K.,Synthesis, spectral, redox and antimicrobial activities of Schiff base complexes derived from 1-phenyl-2,3-dimethyl-4-aminopyrazol-5-one and acetoacetanilide, Transition Met. Chem.,2001,26, 131-135.

\*\*\*\*\*