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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF COORDINATED COMPOUND OF FLUPIRTINE BASE BEARING ORTHO-VANILLIN MOIETY

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ABSTRACT

In the present synthesis Cu(II), Ni(II), Co(II), and Zn(II) complexes of (E)-ethyl 6-(4-fluorobenzylamino)-2-2 hydroxy-3-methoxy benzylidene -amino)pyridine-3yl-carbamate is reported. The structure was confirmed by IR, ESI Mass, UV spectroscopy, Thermal Gravimetric Analysis. Antimicrobial activity against the bacterial and fungal strains was tested.

KEYWORDS: Complexes, Antimicrobial activity, Thermal Gravimetric Analysis, Spectroscopy, strains.

INTRODUCTION

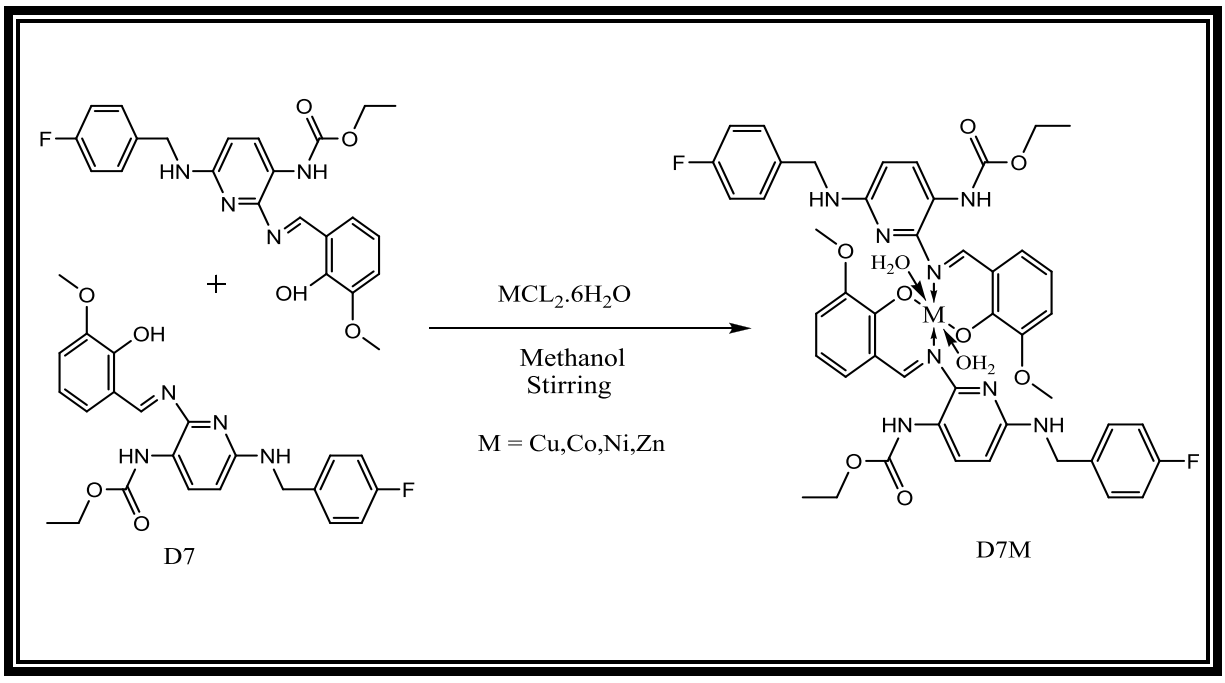
There has been vast interest in metal complexes have been for many years. In the coordination of metals it's known that Nitrogen atom play a key role at the active sites of various molecules,[1] Because of the industrial, antibacterial, antiviral antifungal, anticancer, and herbicidal applications Schiff base metal complexes have been extensively studied.[2-7] It is also use in some important biological species and locates applications in many catalytic reactions.

Since middle of the nineteenth century Schiff base metal complexes have been acknowledged[8] and the general synthesis of the Schiff bases ligands also. Schiff base metal complexes have engaged the essential part in growth of coordination chemistry.

Transition metal complexes which having S, N and O, N donor atoms have large biological activity and lots of information in the chemistry. The metal complexes which donate nitrogen and oxygen to Schiff bases acquire susceptible to molecular environment odd configuration and are structural accountability.[9] The situation in the region of the centre of metal ‘‘lots of coordinated compounds and their donor group, likewise coordination geometry,’’ is the solution for metal protein to bring out definite function of physiology.[10]

MATERIALS AND METHODS

Silica gel (Merck) used to access the synthesized compounds purity by thin layer chromatography. IR spectra were recorded on IR analysis were done with Shimadzu FT-IR-8400, ESI-Mass was done with WATERS,Q-TOF MICROMASS(LC-MS),ESI (Electro spray Ionization) is the ionization techniques for soft ionization of broad range of polar analytes. The U.V. analysis of the synthesized compounds was carried out by Pharma spec UV-1700 Simadzu UV1700, in TGA and DTA for the compounds have been carried out by utilizing Perkin Elmer from room temperature to 900^0C under rate of heating of 10^0C/minute. Magnetic moment of the compound measured by GOUY balance by Hg [Co(CNS)] as standard.



EXPERIMENTAL

The Schiff base was prepared by the condensation of the o-vanillin and flupirtine in 1:1 mole ratio by using methanol.

Synthesis of copper(II), nickel(II), cobalt(II) and zinc(II) complexes of (E)-ethyl 6-(4-fluoro-benzylamino)-2-(2-hydroxy-3-methoxy benzylidene-amino)-pyridine-3-yl-carbamate

A mixture of the corresponding metal chloride (hydrated) (0.01 M) was dissolved in minimum quantity of methanol and added to the solution of 2-hydroxy substituted Ligand (0.02 M) in Methanol and amount of 0.1% KOH in Methanol was added to neutralize pH. The reaction mass was stirred at 25-35^{0}C (for 12 to 24 hr) accorded solid mass separated out. The precipitate was filtered, washed with methanol and dried under vacuum. The metal estimated was carried out by standard methods.

Table-1

No	M.F	M.W	Yield%	Color	Magnetic moment μ_{eff} B.M	Geometry	Magnetism
D7M1	$C_{46}H_{48}CuF_2N_8O_{10}$	973.28	72	Brown	1.83	Octahedral	Paramagnetic
D7M2	$C_{46}H_{48}ZnF_2N_8O_{10}$	976.33	71	Orange	-	Octahedral	Diamagnetic
D7M3	$C_{46}H_{48}NiF_2N_8O_{10}$	969.61	75	Orange	3.12	Octahedral	Paramagnetic
D7M4	$C_{44}H_{48}CoF_2N_8O_{10}$	969.85	74	Brown	4.80	Octahedral	Paramagnetic

Copper(II) complex of (E)-ethyl 6-(4-fluoro-benzylamino)-2-(2-hydroxy-3-methoxy benzylidene-amino)-pyridine-3-yl-carbamate (D7M1)

- **ESI Mass** m/z: 972.26
- **Elemental analysis:**

Calculated Carbon: Carbon: 56.70 ; Hydrogen : 4.96 ; Nitrogen:11.50; Oxygen : 16.42 %

Obtained Carbon: Carbon : 56.90; Hydrogen : 4.87; Nitrogen, 11.31; Oxygen, 16.01%.

- **IR spectra**: 1580 (C=N starching of imine group), 1262 (C-N starching), 1222 (C-O-C straching), 3392 (N-H amide straching), 1007 (-OCH_3 straching), 1510 (C=C of aromatic skeleton),1715 (C=O amide straching), 592 (M–N), 494 (M–O).
- **UV-Vis: (DMF)** (λmax/ nm): 298,354
- **TGA wt. loss in %(temp.):** 1.95 (100^{0}C); 10.66 (200^{0}C); 23.89 (300^{0}C); 35.50 (400^{0}C); 44.47 (500^{0}C); 54.19 (600^{0}C); 63.77 (700^{0}C); 72.25 (800^{0}C); 79.78 (900^{0}C)

Zinc complexe of (E)-ethyl 6-(4-fluoro benzyl amino)-2-(2-hydroxy -3-methoxy benzylideneamino) pyridine-3-ylcarbamate (D7M2)

- **Elemental analysis:**
  Calculated Carbon:Carbon: 56.59; Hydrogen: 4.96; Nitrogen:11.48; Oxygen : 16.39 %
  Obtained Carbon:Carbon: 56.70; Hydrogen : 4.97; Nitrogen, 11.41; Oxygen, 16.43%
- **IR spectra**: 1583 (C=N starching of imine group), 1273 (C-N starching), 1234 (C-O-C straching), 3372 (N-H amide straching), 1008 (-OCH_3 straching), 1512 (C=C of aromatic skeleton),1720 (C=O amide straching), 573 (M–N), 510 (M–O).
- **UV-Vis: (DMF)** (λmax/ nm): 252,302
- **TGA wt. loss in %(temp.):** 1.15 (100^{0}C); 5.76 (200^{0}C); 16.55 (300^{0}C); 27.55 (400^{0}C); 35.70 (500^{0}C); 48.93 (600^{0}C); 59.07 (700^{0}C); 68.54 (800^{0}C); 78.04 (900^{0}C)

Nickel complexe of (E)-ethyl 6-(4-fluoro benzyl amino)-2-(2-hydroxy -3-methoxy benzylideneamino) pyridine-3-ylcarbamate (D7M3)

- **Elemental analysis:**
  Calculated Carbon:Carbon: 56.98; Hydrogen : 4.99 ; Nitrogen:11.56; Oxygen : 16.50 %
  Obtained Carbon : Carbon:56.90; Hydrogen : 4.97; Nitrogen, 11.61; Oxygen, 16.61%
- **IR spectra**: 1581 (C=N starching of imine group), 1258 (C-N starching), 1220 (C-O-C straching), 3393 (N-H amide straching), 1009 (-OCH_3 straching), 1512 (C=C of aromatic skeleton),1707 (C=O amide straching), 592 (M–N), 492 (M–O).
- **UV-Vis: (DMF)** (λmax/ nm): 256,318
- **TGA wt. loss in %(temp.):** 10.57 (100^{0}C); 15.26 (200^{0}C); 18.92 (300^{0}C); 29.61 (400^{0}C); 52.57 (500^{0}C); 87.75 (600^{0}C); 88.28 (700^{0}C); 88.66 (800^{0}C); 89.12 (900^{0}C)

Cobalt complexe of (E)-ethyl 6-(4-fluoro benzyl amino)-2-(2-hydroxy -3-methoxy benzylideneamino) pyridine-3-ylcarbamate (D7M4)

- **Elemental analysis:**
  Calculated Carbon: Carbon: 56.97 ; Hydrogen : 4.99 ; Nitrogen:11.55; Oxygen : 16.50 %
  Obtained Carbon: Carbon : 57.10; Hydrogen : 4.90; Nitrogen, 11.31; Oxygen, 16.55%
- **IR spectra**: 1581 (C=N starching of imine group), 1261 (C-N starching), 1224 (C-O-C starching), 3394 (N-H amide starching), 1001 (-OCH_3 starching), 1514 (C=C of aromatic skeleton),1723 (C=O amide starching), 588 (M–N), 500 (M–O).
- **UV-Vis: (DMF)** (λmax/ nm): 256,308

- **TGA wt. loss in %(temp.):** 2.18 (100^0C); 10.25 (200^0C); 21.52 (300^0C); 34.76 (400^0C); 42.69 (500^0C); 51.23 (600^0C); 59.80 (700^0C); 67.87 (800^0C); 75.04 (900^0C).

RESULTS AND DISCUSSION

The elemental analysis of the (E)-ethyl 6-(4-fluoro benzyl amino)-2-(2-hydroxy -3-methoxy benzylideneamino) pyridine-3-ylcarbamate's four metal complexes of Copper, Nickel, Cobalt and Zinc were shown by found percentages and were matched with calculated.

For the all four Metal complexes confirmatory Coordinate bands for C=N of Schiff base group were comes at 1575 cm-1 which was slightly shifted from it corresponding Schiff bases value. In all the complexes suggest that the ligands coordinated to the metal ion through C-N 1250-1273 cm-1 correspondingly. Another characteristic C-O 1220-1240 carbonyl starching was observed at 1707-1723 cm-1, N-H starching of NH2 was observed at 3372-3394 While the –OH bond disappeared. New absorption bands ν(M-N) and ν(M-O), appeared at 573-592 cm -1and 492-510 cm-1 respectively,This suggested formation of desired products.

In case of all four metal complexes the curved showed first weight loss corresponding to coordinate water molecules in the temperature range of 50 to 200^{o}C. The presence of water molecules in the metal chelates have also been supported by IR studies. By UV study The absorptionbands below 300 nm shows in all synthesized compound shows practically π→π* transitions in the benzene ring and the absorption bands observed between 300 and 400 nm range are due to the n→ π* transitions of imine groups. All the synthesized metal chelates are decomposed in two stages. The first stage with loss of the total weight is due to the removal of water molecules. The second stage corresponds to the decomposition of ligand. Even after end of the decomposition some percentage of the compound is remained which showed the presence of the metal ions in the compounds. By Magnetic Susceptibility data we can conclude the metal complexes of the Cu, Ni and Co are paramagnetic behaviour but the metal complexes of Zn are Diamagnetic.The data shows that the Copper complexes contains 1.75 to 1.93 BM value, The Nickel complexes give the results between 2.8 BM to 3.5 BM, The Cobalt complexes given values between 4.72 to 4.86 but the Zinc Complexes given no value in Gouy balance.

Table-2.MIC against different bacteria (in μ_g)

No	*E*. coli	P. aeruginosa	S. aureus	B. subtilis
D7M1	>800	>800	800	>800
D7M2	400	>800	>800	>800
D7M3	800	800	>800	>800
D7M4	400	400	300	300
CIPROFLOXACIN	15	10	15	05

Table-3.MIC against fungi (in μ_g)

No	Candida albicans
D7M1	>800
D7M2	400
D7M3	400
D7M4	200
FLUCONAZOLE	10

CONCLUSION

In this paper, Cu(II), Co(II), Ni(II) and Zn(II) complexes of (E)-ethyl 6-(4-fluorobenzylamino)-2-2 hydroxy-3-methoxy benzylidene -amino)pyridine-3yl-carbamate were synthesized and characterized by spectral techniques. The electronic spectral studies of the four complexes indicate the square planar geometry for the metal ions.

BIOLOGICAL ACTIVITY

"**KIRBY-BAUER TECHNIQUE**" used to estimate the antibacterial and antifungal activity of these synthesized compounds. Both methods primary and secondary were used for the monitoring antimicrobial activity of coordinated compounds.

The synthesized compounds were screened through different types of screening. From the results it is obvious that all the synthesized ligand and metal complexes are having moderate activity at lower concentration. From Metal complexes D7M1,D7M2 and D7M3 showed moderate activity and D7M4 Showed somewhat good activity towards Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Bacillus Subtilis, For Antifungal agent D7M2,D7M3 and D7M4 showed somewhat good activity towards Candida albicans. All the metal complexes showed the moderate activity compares to standard.

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