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Synthesis, Characterization and Antimicrobial Screening of Some Selected 3D Transition Metal (Fe(iii), Co(ii), Ni(ii), Cu(ii) & Zn(ii)) Complexes Derived from (12e)-N-((6-Chloro-4-Oxo-4h-Chromen-3-Yl) Methylene)-4-Methyl-1,2,3,-Thiadiazole-5-Carbohydrazide

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ABSTRACT

A novel Schiff base (12E)-N-((6-chloro-4-oxo-4H-chromen-3-yl)methylene)-4-methyl-1,2,3,-thiadiazole-5-carbohydrazide obtained by the condensation of 6-chloro-4-oxo-4H-chromene-3-carbaldehyde and 4–Methyl-1,2,3,-thiadiazole-5-carbohydrazide and and the synthesized schiff base was characterized by various analytical technique such as I.R., 1H-NMR, 13C-NMR and. Further it used for the complexation with different transition metal ions such as Fe (III), Co(II), Ni (II), Cu(II) and Zn (II) by using molar ratio of metal to ligand as 1: 2. The prepared metal complexes were identified with the help of FT-IR, elemental analysis, and TGA methods. The spectral data reveal that the ligand acts as bidentate, tridentate in ML complexes. The effect of these metal complexes on bacterial and fungal species was studied and compared with those of free ligand. The results of antimicrobial studies show enhanced activity in comparison to the free ligand.

Keywords: NO,ONO donor Schiff base; Fe(III),Co(II), Ni(II), Cu(II) and Zn(II) complexes; spectroscopic analysis; antimicrobial activity.

I. INTRODUCTION

Chromone hydrazones are extremely promising ligands in coordination chemistry [1]. They are also important in catalysis and in medicine as antimicrobial, antioxidant and anticancer agents [2]. Metal complexes of hydrazone ligands have been widely studied over earlier periods.Variety of hydrazones which can be prepared by condensation of different kinds of hydrazides and carbonyl compounds, hydrazones derived from chromone compounds have been the center of attraction for numerous workers in current scenario. The chromone moiety execute as the vital constituent in lots of pharmacophores of biological active molecules of synthetic as well as natural origin and many of them have useful medicinal applications .

chromone resides in an exclusive position for two reasons. They are carrying a substantial biological activity and they are prominent synthetic intermediates [3-5]. The notable biological properties, proton affinities, optical properties and the degree of aromaticity of the chromones have paying attention from both theoretical and experimental point of views. The 3-formylchromones have several applications. They are used as adaptable synthons in heterocyclic chemistry[6-10] . In the pharmaceutical area, the effectiveness and selectivity of derivates of 3-formylchromones, provides a novel pharmacophore for the design of drugs for the treatment of type II diabetes and obesity[11-12]. Work has shown that some drugs are evidence for improved action when administered as metal chelates rather than as organic compounds and that the coordinating power has been enhanced by condensing with a variety of carbonyl compounds.

II. EXPERIMENTAL

2.1 Materials

All the purchased chemicals were analytical grade and used without further purification. Solvents were purified and dried according to literature method[13-14]. All chemicals were obtained from Sigma–Aldrich chemical used without purification. They included 6-fluoro-4-oxo-4H-chromene-3-carbaldehyde and 4–Methyl-1, 2,3,-thiadiazole-5-carbohydrazide, remaining all chemical solvents were purchased from spectrochem ltd.

2.2 Physical measurements

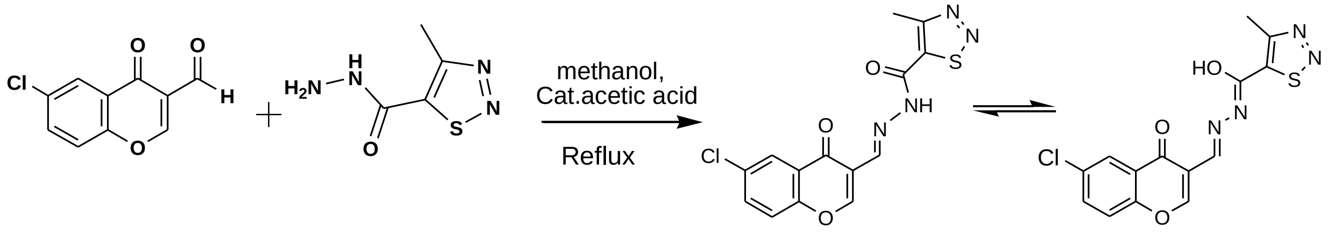
Elemental analysis (C, H, N,) was performed using Perkin Elmer CHN analyzer. IR spectra of the ligands and their metal complexes were recorded on Bruker spectrometer within the range of 4000–400 cm^{-1}. Thermal studies of the complexes were carried out on a Perkin Elmer diamond TGA instrument. ^{1}H-NMR and ^{13}C-NMR spectra of the ligands were recorded on Bruker spectrometer using DMSO-d6 as a solvent and TMS as internal standard. Mass spectra were recorded on water, Qt of micromass (ESI-MS).

2.3 Synthesis of the Schiff base ligand

The Schiff base ligand was prepared by condensation of 6-chloro-4-oxo-4H-chromene-3-carbaldehyde (1.00 mmole) and 4 – Methyl-1,2,3,-thiadiazole-5-carbohydrazide (1.00 mmole) in absolute ethanol (20 ml), 3-4 drops of acetic acid. The mixture was refluxed for 6-7 hr with continuous stirring. The progress of reaction was monitored by TLC and after completion of the reaction; the mixture was poured on crushed ice and filtered off. The obtained product was recrystallized in absolute Methanol.

2.4 Spectral data of ligand:

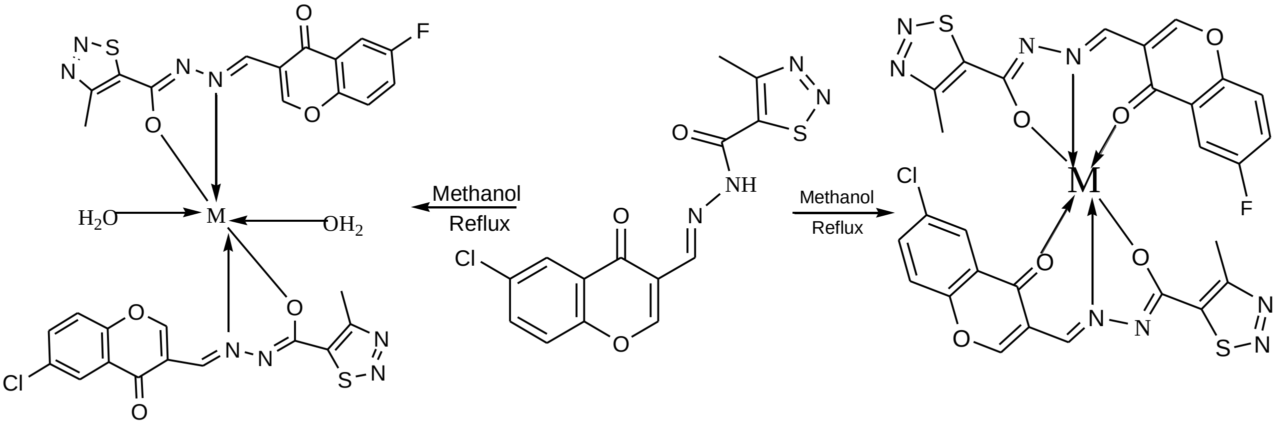
Color: Spongy white , Yield: 77 %, M.P.: 278 °C, Selected FT-IR bands (KBr, cm^{-1}) : 3191.92 ν (NH), 1665 ν(C=O chromone), 1625 ν (C=O hydrazonic), 1574 ν(C=N); ^{1}H- NMR (DMSO-d6, δ ppm) 12.36 (1H,s, iminolic -OH); 8.47 (S, 1H, HC=N), 6.94-8.26 (m, 4H, Ar-H); 2.98 (S, 3H, $-CH_3$); ^{13}C- NMR (DMSO-d6, δ ppm) 163.63 (C=O chromone), 160.38 (C=O hydrazone), 155.98 (-HC=N), 15.39($-CH_3$);



Scheme: The schematic route for synthesis of Schiff base (L)

2.5 Synthesis of metal complexes

The Schiff base ligand L (0.01 mol) is dissolved in hot methanol solution of corresponding salts (0.005 mol) MX2 [where M= Fe(III),Co(II), Ni(II), Cu(II), and Zn(II)] were mixed together and refluxed with constant stirring for 6–8h at refluxing temperature. On cooling colored solids were precipitated out. The products were filtered, washed with cold methanol, dried in air and in desiccator over anhydrous $CaCl_2$ and stored in an airtight sample bottle. All the compounds are colored and are stable to air and moisture.



M= Fe(III),Ni(II)

L

M = Co(II), Cu(II), Zn(II),

III. RESULTS AND DISCUSSION

The analytical data and physical properties of the ligand and its metal complexes are listed in Table 1. The Schiff base ligand (L) is soluble in common organic solvents. The resultant Schiff base complexes are partially soluble in MeOH and $CHCl_3$ but freely soluble in DMF and DMSO. The analytical data indicate that the metal to ligand ratio is 1:2 in all the metal complexes.

Compound	Mol. Formulae (F.W.)	M.P. °C	Colour	Elemental analysis found (calculated.)%			
				% C (cal.)	% H (cal.)	% N (cal.)	% M (cal.)

Ligand (HL)	$C_{14}H_9FN_4O_3S$ (314.05)	256°C	Brown	58.98 (50.60)	2.68 (2.73)	16.08 (16.86)	-
$[Fe(HL)_2(H_2O)_2]$	$C_{28}H_{20}Cl_2FeN_8O_8S_2$	>280 °C	Green	44.88 (46.61)	2.98 (2.24)	15.10 (15.54)	7.78 (8.18)
$[Co(HL)_2]$	$C_{28}H_{16}Cl_2CoN_8O_6S_2$	>280 °C	Coffee	45.33 (46.61)	2.06 (2.24)	14.56 (15.53)	7.66 (8.14)
$[Ni(HL)_2(H_2O)_2]$	$C_{28}H_{20}Cl_2NiN_8O_8S_2$	>280 °C	Brown	42.14 (44.41)	2.40 (2.66)	14.12 (14.85)	7.10 (7.78)
$[Cu(HL)_2$	$C_{28}H_{16}CuCl_2N_8O_6S_2$	>280 °C	Brown	44.35 (46.31)	2.10 (2.22)	14.68 (15.43)	8.30 (8.76)
$[Zn(HL)_2$	$C_{28}H_{16}Cl_2ZnN_8O_6S_2$	>280 °C	Brown	45.77 (46.20)	2.06 (2.22)	14.68 (15.39)	8.38 (8.88)

Table-1: Physical and analytical data of L and its metal complexes.

3.1 FT-IR spectra

The IR spectra containing relevant vibrational bands of the ligands and their metal complexes are listed in Table 2.

Compound Name	ν(C=O) Chromone	ν(C=O) hydrozonic	ν(C=N)	ν(M-O)	ν(M-N)
L	1665	1625	1505	-	
$[Fe(L)_2(H_2O)_2]$	1656	1603	1533	522	416
$[Co(L)_2]$	1658	1612	1537	528	450
$[Ni(L)_2(H_2O)_2]$	1659	1605	1562	538	460
$[Cu(L)_2$	1661	1604	1565	518	470
$[Zn(L)_2$	1656	1603	1536	546	426

Table-2: The selective Infrared frequencies of ligand (HL) and its metal complexes

The ligands showed a band at 1665 cm^{-1} which is due to ν (C=O) group of the chromone moiety. This band was shifted to lower wave number region 05–10 cm^{-1} in their corresponding metal complexes, indicating the coordination of oxygen atom of carbonyl group of the chromone moiety. The stretching vibration of the azomethine group (C=N) was observed at 1505 cm^{-1} in the ligand. This band was shifted to lower wave number region 20-40 cm^{-1} in their metal complexes, indicating the participation of nitrogen atom of azomethine group in coordination to the metal ion. An appearance of new broad band in the region 3253-3397 cm^{-1} indicates the presence of coordinated water in Fe(III),Ni(II), metal complexes. The coordination of nitrogen and oxygen atoms was supported by the appearance of a non-ligand bands in the range 500-550cm^{-1} and 416-470 cm^{-1} region due to the ν(M–O) and ν(M–N), respectively. From the above spectral data, it was concluded that schiff base ligand acts as bidentate in Fe(III) and Ni(II) metal complexes due to coordination of two water molecule and tridentate ligands in Cu(II), Co(II), and Zn(II) metal complexes with ONO donor sites.

3.2 ^{1}H-NMR spectra

The ^{1}H-NMR and ^{13}C- NMR spectrums of ligand was recorded in DMSO-d6 ^{1}H- NMR (DMSO-d6, δ ppm) 12.36 (S, 1H, NH); 8.47 (S, 1H, HC=N), 6.94-8.26 (m, 4H, Ar-H); 2.98 (S, 3H, $-CH_3$); ^{13}C- NMR (DMSO-d6, δ ppm) 163.63 (C=O chromone), 160.38 (C=O hydrazone), 155.98 (-HC=N), 15.39($-CH_3$);

3.3 Thermogravimetric analysis

Thermal analysis was used mainly for the confirmation of the water molecule or solvent associated with being in the sphere of coordination or in the outer sphere of the complex [15-16]and the information about its properties, the nature of the products intermediate and final thermal decomposition. From the TGA curves, the weight loss was calculated for the different steps and compared with the theoretically calculated weight for the suggested formulas based on the results obtained from the elemental analyzes. Thermal stability of the synthesized metal complexes was done up to 900 °C at a heating rate of 10 °C/min in nitrogen atmosphere. Metal complexes exhibit similar decomposition pattern as evident from their TGA graphs. The TGA graph shoes that decompose of Fe metal complex in three steps within temperature range of 10–700 °C. First step corresponds to the loss of two coordinated water molecules (Found 03.98 %, calcd. 04.77 %) in temperature range of 10–160 °C. The second step corresponds to the loss of $(C_{11}H_6ClN_2O_2)_2$ (Found 56.78 %, calcd. 57.82 %) in temperature range of 160–400 °C. A peak corresponding to mass loss of (25.36% calcd.27.50 %) at 400-650 °C was due to the loss of $(C_3H_3N_2S)_2$in the third step and as a final product, it leaves FeO as residue. Similar behavior was observed in the TGA curve of metal complexes 3-4. Thermal analysis data of all metal complexes (2-4) collectively given in Table 3.

Comp .no.	Molecular formula	Stages	Temp (°C)	Possible evolved species	Residual species	Mass loss	
						Found	Calc.
1	$[Fe(L)_2(H_2O)_2]$	1st 2nd 3rd	10-160 ^{0}C 160-400 ^{0}C 400-600 ^{0}C	2 H_2O $(C_{11}H_6FN_2O_2)_2$ $(C_3H_3N_2S)_2$	FeO	03.98 56.78 25.36 09.10	04.77 57.82 26.25 09.41
2	$[Co(L)_2]$	1st 2nd	10-320 ^{0}C 320-650 ^{0}C	$(C_{11}H_6FN_2O_2)_2$ $(C_3H_3N_2S)_2$	CoO	59.14 25.68 09.22	60.55 27.50 10.27
3	$[Ni(L)_2(H_2O)_2]$	1st 2nd 3rd	10-190 ^{0}C 190-400 ^{0}C 400-700 ^{0}C	2 H_2O $(C_{11}H_6FN_2O_2)_2$ $(C_3H_3N_2S)_2$	NiO	4.14 56.28 25.44 9.10	4.76 57.60 26.19 09.65

Table 3: Thermal analysis data of metal complexes

3.4 Antimicrobial activity

The in vitro antimicrobial screening of synthesized ligand and metal complexes was tested against four bacteria (*S. Aureus, S. Pyogenes, E. Coli & S. Typhi*) and two fungi (*C. Albicans & T. Rubrum*) by petri-plate containing 30 ml potato dextrose agar and nutrient agar medium, the plates were incubated for 20-24 hr and 24-48 hr for bacteria and fungi stains, respectively. The activities were measured in terms of zone of inhibition in mm. Cefotaxime, Azithromycin and Clotrimazole were used as standard drugs for bacteria and fungi, respectively at 500 ppm concentration of sample as well as drugs. The results of antimicrobial activity of ligand and metal complexes are shown in Table 4.

The metal complexes exhibit higher inhibition against tested microorganism compared to the free ligand[17-18]. The value in the above table indicates that the activity of the Schiff base ligand became more pronounced when coordinated with the metal ions. The presence of azomethine moiety and chelation effect with central metal enhances the antibacterial activities. This enhancement in antibacterial activity of these metal complexes can be explained based on the chelation theory[19-21].

When a metal ion is chelated with a ligand, its polarity will be reduced to a greater extent due to the overlap of ligand orbital and the partial sharing of the positive charge of the metal ion with donor groups. Furthermore, the chelation process increases the delocalization of the π-electrons over the whole chelate ring, which results in an increase in the lipophilicity of the metal complexes. Consequently, the metal complexes can easily penetrate into the lipid membranes and block the metal binding sites of enzymes of the microorganisms. These metal complexes also affect the respiration process of the cell and thus block the synthesis of proteins, which restrict further growth of the organism. The results of antimicrobial activity of ligand and metal complexes are shown in factors. They are the chelate effect, nature of coordinated ligand, total charge of complex, nature of the ion neutralizing the ionic complex and nuclearity of the metal center in the complex[22-24].. The increased activity of the metal complex than the free ligand can also be explained on the basis of chelation theory.

Compounds	Zone of Inhibition in mm					
	Gm +ve bacteria		Gm -ve bacteria		Antifungal activity	
	S. Aureus	S. Pyogenes	E. Coli	S. Typhi	C. Albicans	T.Rubrum
Ligand (HL)	7	6	8	9	-	-
$[Co(HL)_2]$	12	14	8	10	16	14
$[Ni(HL)_2(H_2O)_2]$	-	-	11	12	-	-
$[Cu(HL)_2]$	14	16	8	10	14	16
$[Zn(HL)_2]$	9	12	10	11	11	10
Cefotaxime	-	-	26	22	-	-
Azithromycin	26	24	-	-	-	-
Clotrimazole	-	-	-	-	16	15

Table 4: Results of antimicrobial activity of synthesized compounds

IV. CONCLUSION

In the present work, Fe(II), Co(II), Ni(II) ,Cu(II),and Zn(II) complexes were prepared from 6-fluoro-4-oxo-4H-chromene-3-carbaldehyde and 4- Methyl-1,2,3,-thiadiazole-5-carbohydrazide These Schiff base are characterized using various spectral techniques. IR spectra revealed coordination of Schiff base ligand with metal ion through azomethine nitrogen, carbonyl oxygen of chromone moiety and carbonyl oxygen of hydrazide moiety. The structural elucidation studies by various spectral techniques (IR, and ^{1}H NMR) suggested the nature of ligand is bidentate in Fe(III) and Ni(II) metal complexes due to coordination of two water molecule and tridentate ligands in Cu(II), Co(II), and Zn(II) metal complexes with ONO donor sites tridentate and geometry of the metal complexes are octahedral. Thermogravimetric analysis studies demonstrate the stability of complexes as well as provided the number of coordinated water molecules. Antimicrobial studies suggest that Schiff base and its complexes play a vital role in developing a new class of antibiotics.

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