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Synthesis, characterization and biological activity of new metal complexes of N-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide.

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ABSTRACT

Seven metal complexes derived from *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)-acetamide (hydrazide of paracetamol) were prepared and characterized. Different standardized instruments were used for obtaining the required data (spectral method UV-vis., IR, ¹H-NMR, mass spectra) magnetic susceptibility and thermogravimetric analysis TGA were performed. The electronic spectral data and magnetic moment values proved that all the metal complexes except copper (II) and vanadium (IV) complex have octahedral geometry, whereas copper complex has square planar structure and vanadium complex has square pyramidal . Antibacterial screening of the ligand and its complexes against *Escherichia coli* (E.coli) and *Staphylococcus aureus* (S. aureus), was also investigated. The ligand and its metal complexes were found to have varied degree of inhibitory effect against the bacteria. The results obtained proving the potentials of these compounds as broad-spectrum antimicrobial agents.

Keywords: Paracetamol hydrazide, chelate complex, antimicrobial activities.

INTRODUCTION

Acetaminophen (paracetamol) is the most widely used as a pharmaceutical analgesic and antipyretic agent [1]. It was known to be hepatotoxic in man and various experimental animals upon overdose [2–4]. Taking the presumed molecular mechanisms of analgesic activity as well as of the hepatotoxicity of paracetamol into consideration, there have been several efforts to improve its analgesic activity while preventing its toxicity by modifying its structure [5–8].

However, it is known that some drugs act via chelation or by inhibiting metalloenzymes but for most of the drugs that act as potential ligands, a lot of studies are being carried out to ascertain how metal binding influences the activities of the drugs [9].

Metal complexes are gaining increasing importance in the design of drugs on coordination with a metal. This has led to lots of study on metal drug complexes. The formation of complexes of paracetamol and Zn(II) was studied in aqueous media at pH 7.2 by polarography and spectroscopy [10]. The stoichiometry of the Zn(II)-paracetamol complex was 1:1. Analgesic studies on the drug and its metal complex have been performed in albino mice. Revealing the complex to be more potent in analgesic activity compared to the paracetamol alone drug.

The complexation between metal ions like (Cd(II), Hg(II) and Pb(II) with Para produced 1:2 M ratio (metal: Para) as a monodentate via hydroxyl group. The antimicrobial activities of the metal complexes of Para recorded a significant effect against some bacteria and fungi [11].

Complexes of paracetamol with various metal ions such as, Cu(II), Zn(II) or Fe(II) ions of ratio 2:1, respectively, have been prepared and their structure has been confirmed by elemental analysis, atomic absorption spectra, IR spectra and ^1H NMR spectra in which two paracetamol molecules are chelated to any one of the metal ions, Cu(II), Zn(II) and Fe(II) ions [12].

Complexes of Mg(II), Ca(II), Ba(II) and Sr(II) with paracetamol drug were synthesized and characterized by elemental analysis, conductivity, UV–Vis, IR, and ^1H NMR spectroscopy and thermal analysis, as well as screened for antimicrobial activity. From the microanalytical data, the stoichiometry of the complexes reacts with Mg(II), Ca(II), Ba(II) and Sr(II) by molar ratios (2:1) (paracetamol: metal ion). The thermal behavior (TG/DTG) of the complexes was studied. The ligand and their metal complexes were screened against both of antibacterial and fungicidal activities. These complexes are found to have high activity against bacteria and fungi [13].

Obaleye and Lawal [14] reported the synthesis and antibacterial studies of some Aspirin and Paracetamol metal complexes. The complexes were found to have higher activities than the original Aspirin and Paracetamol.

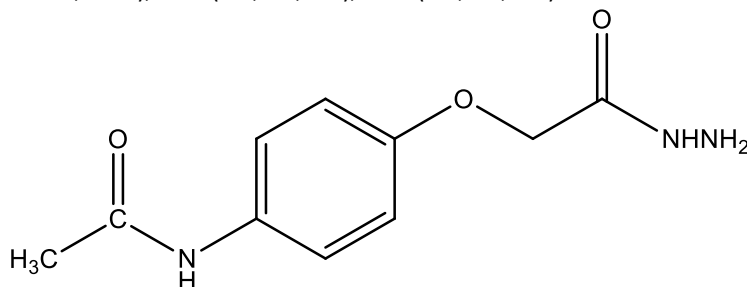
Ibuprofen and paracetamol form several complexes with metal (II) ions. The synthesis and properties of these types of compounds was investigated. The structures of the complexes of Ibu and Par with Mn(II), Co(II), Fe(III) and Cu(II) have been confirmed from the elemental analysis, FT-IR spectroscopy and thermal analysis. Thus, from the FTIR spectrum, it is concluded that both Ibu and Par behave as a monobasic bidentate ligand coordinated to the metal ion. The thermal investigation (studied by TG/DTG techniques) shows that obtained complex decomposes progressively. The final product of the thermal decomposition is metal oxides, which through its percentage confirms the empirical formulae of the new complexes prepared. The paracetamol complexes were found to have high activity against *Bacillus subtilis* and penicillium, whereas the Fe(III) complex was more active than the Mn(II), Co(II) and Cr(III) complexes against *trichoderma* [15].

In the present work a number of new metal complexes of copper(II), manganese (II), chromium(III), iron (III), Zink(II), cobalt(II), and vanadium(IV) with a new hydrazone ligand *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)-acetamide (HL) is prepared. The chemical formulations of ligand and its metal complexes were characterized using elemental analysis, spectral measurements (UV-Vis, IR), ^1H NMR, mass spectra, magnetic susceptibility and thermal analyses.

EXPERIMENTAL

Synthesis of *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide (HL)

A mixture of ethoxycarbonylmethylparacetamol (2.37g, 0.1 mole), hydrazine hydrate (1.5 g, 0.3 mole) and ethanol (30 ml) was heated under reflux for 5h (TLC). The product was filtered off, recrystallized from ethanol to yield white needles in 90% yield. White needles (90%), m.p. 145-147°C $R_f = 0.31$ (5% MeOH in CH_2Cl_2). ^1H NMR ($\text{DMSO}-d_6$): $\delta = 2.04$ (s, 3H, CH_3), 2.00 (brs, 2H, NH_2), 4.63 (s, 2H, CH_2), 6.97 (d, 2H, $J = 5.5$ Hz, Ar-H), 7.51 (d, 2H, $J = 5.5$ Hz, Ar-H), 7.23 (brs, 1H, NH), 8.00 (brs, 1H, NH).



Preparation of the complexes

The complexes were prepared by adding an equimolar (1M:1L) ethanolic solution of $\text{MCl}_2 \cdot n\text{H}_2\text{O}$ ($\text{M} = \text{Cu(II)}, \text{Mn(II)}, \text{Cr(III)}, \text{Fe(III)}, \text{Zn(II)}, \text{Co(II)}$ and V(IV) ; $n = 0-6$) to a hot solution of ligand. The reaction solution was stirred for few hours at 90°C and then cooled. The formed complex was filtered off, washed several times with ethanol and dried under vacuum over P_4O_{10} .

Physical measurements for ligand and its metal complexes

Elemental analyses (C, H, N, and Cl) were performed at the Micro-analytical Unit of the University of Cairo. Metal analyses were carried out by back titrating method 20mL of a neutral metal complex solution (after a complete decomposition by using concentrated nitric acid) with 0.01M EDTA solution using Eriochrome Black T indicators.

The electronic spectra were measured in Nujol mulls using a Perkin Elmer Lambda 4B spectrophotometer.

The thermogravimetric analysis TGA was carried out under N_2 atmosphere using Shimadzu TGA-50. Magnetic susceptibilities were measured at room temperature by a modified Gouy method using a Johnson Matthey magnetic susceptibility balance. Diamagnetic corrections were made using Pascal's constants [16].

The magnetic moments were calculated from the equation $\mu_{\text{eff}} = 2.84(\chi_M^{\text{corr}} T)^{1/2}$.

Microbiological investigation

Hole well method

The investigated isolates of bacteria were seeded in tubes with nutrient broth (NB) two different bacteria species were used *Escherichia coli* (E.coli) and *Staphylococcus aureus* (S. aureus).

Antimicrobial activity of chemical compounds was evaluated by Hole well method, Briefly ,inoculum containing approx. cell density (1.5×10^8 CFU/ml) was spread on Mueller-Hinton agar (MHA) plates the holes diameter (0.5 cm) were done in the cool medium after that 50μ from different concentration of compounds 10, 20 and 30 mg/mL of each ligand and its metal complex in DMSO was introduced into the wells and the plates were allowed to stand on the bench for 30 minutes before incubation at 37°C for 24 hours after which inhibitory zones (in mm) were taken by using a micropipette as a measure of antimicrobial activity.

The previous procedure was repeated with 30 µg/disc of tetracycline and with ampicillin at 10 µg/disc [17], which they were used as the reference drugs.

RESULTS AND DISCUSSION

Characterization of *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide (HL) and Its metal complexes

Table (1) shows the color, elemental analyses, stiochiometries of the isolated solid ligand and its metal complexes. The analytical data (Table 1) show that the 1:1 molar ratio reaction of Cu(II), Mn(II), Cr(III), Fe(III), Zn(II) and Co(II) chloride salts and vanadyl sulfate (VOSO₄) salt produced different types of metal complexes of the following formulae [(HL)₂CuCl₂].6.5EtOH.1.5H₂O, [(HL)₂Mn₃Cl₆].3.5EtOH.3H₂O, [(HL)CrCl₃(H₂O)].3EtOH.3H₂O, [(HL)₃Fe₂Cl₄].Cl₂.7EtOH, [(HL)ZnCl₂].0.5EtOH. 0.25H₂O, [(HL)₂CoCl₂].2H₂O and [(HL)₂VO].SO₄ respectively. These are stable metal complexes and non-hygroscopic. All the complexes are freely soluble in *N,N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO-*d*₆). While, in water, ethanol and methanol, they are partially soluble.

Number	Compound	Color, FW	M.P.	Found (Calc.)					λ, Ω ⁻¹ cm ⁻¹
				C	H	N	M	Cl	
HL	C ₁₀ H ₁₃ N ₃ O ₃	White, 223.23	145-147 °C	53.59 (53.75)	5.79 (5.82)	18.69 (18.81)	-	-	-
1	[(HL) ₂ CuCl ₂].6.5EtOH.1.5H ₂ O C ₃₃ H ₆₈ N ₆ O ₁₄ CuCl ₂	Green, 907.499	Above 300°C	43.73 (43.67)	7.03 (7.55)	9.12 (9.26)	7.03 (7.00)	7.92 (7.81)	0
2	[(HL) ₂ Mn ₃ Cl ₆].3.5EtOH.3H ₂ O C ₂₇ H ₄₇ N ₆ O _{12.5} Mn ₃ Cl ₆	Brown, 1039.107	218-220°C	31.22 (31.21)	4.32 (4.55)	7.99 (8.08)	5.12 (5.28)	20.25 (20.47)	0
3	[(HL)CrCl ₃ (H ₂ O)].3EtOH.3H ₂ O C ₁₆ H ₃₉ N ₃ O ₁₀ CrCl ₃	Grey, 592.005	Above 300°C	32.48 (32.46)	6.47 (6.64)	7.05 (7.09)	8.59 (8.78)	17.78 (17.96)	7
4	[(HL) ₃ Fe ₂ Cl ₄].Cl ₂ .7EtOH C ₄₄ H ₈₁ N ₉ O ₁₆ Fe ₂ Cl ₆	Brown, 1316.18	Above 300°C	40.15 (40.12)	6.07 (6.15)	9.44 (9.57)	8.53 (8.48)	16.36 (16.16)	120
5	[(HL)ZnCl ₂].0.5EtOH.0.25H ₂ O C ₁₁ H _{16.5} N ₃ O _{3.75} ZnCl ₂	White, 386.929	270-275°C	34.08 (34.11)	4.12 (4.26)	11.48 (10.85)	16.63 (16.89)	18.17 (18.32)	0
6	[(HL) ₂ CoCl ₂].2H ₂ O C ₂₀ H ₃₀ N ₆ O ₈ CoCl ₂	Bright Red, 612.402	225-230°C	39.71 (39.22)	4.71 (4.93)	16.87 (13.72)	9.69 (9.62)	11.76 (11.57)	0
7	[(HL) ₂ VO].SO ₄ C ₂₀ H ₂₆ N ₆ O ₁₀ SV	Grey, 593.468	Above 300°C	40.97 (40.47)	4.24 (4.41)	14.55 (14.16)	8.94 (8.58)	-	116

Table (1) Analytical data of *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)-acetamide (HL) and its metal complexes.

Mass spectra

The mass spectrum of the ligand (HL) is clear an accurate parent molecular ion peak at *m/z* 223.04 amu, matched with the theoretical molecular weight. The spectrum suggested that the ligand has a monomeric nature. Also, the mass spectrum displayed multiple peaks corresponding to successive degradation of the ligand. The formation of different fragment ions appeared at *m/z* 151, 109, 77 and 65 amu corresponding to [C₈H₉NO₂]⁺, [C₆H₇NO]⁺, [C₆H₅]⁺ and [C₅H₅] respectively.

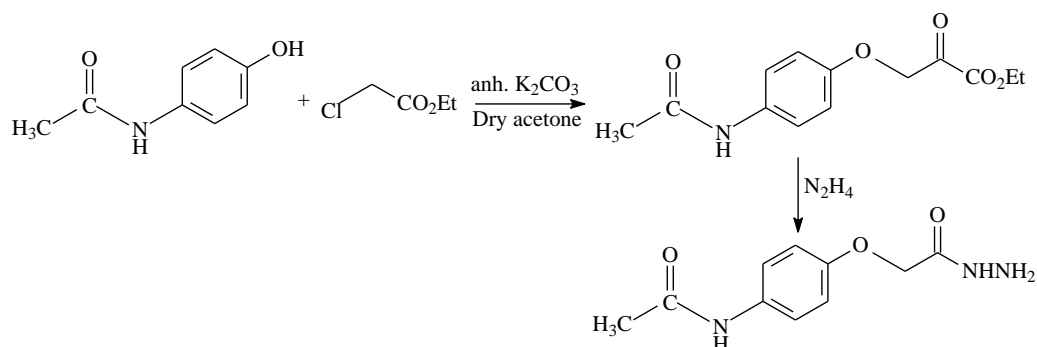
Spectral Studies

Infrared spectra of ligand (HL) and its metal complexes

The fundamental bands of infrared spectrum of ligand are collected in Table (2). The following points are of the major importance for assigning the possible structure of ligand. The spectrum gave strong bands at 3287, 3124, 3045, 1577, 1505, 972 - 925, 830, 743 and 470 cm⁻¹ assigned to ν NH₂ (asym), ν NH₂ (sym), ν NH

(amide), δ NH₂, δ NH (amide), ν (N-N)[18,19], γ NH₂, γ NH amide and ρ NH₂[19], respectively. The carbonyl group characterized by strong bands located at 1642, 520 cm⁻¹ and weak band at 590 cm⁻¹ due to ν (C=O), γ (C=O) and δ (C=O), respectively[19,20]. The presence of fundamental bands due to NH and C=O (ν , δ , γ) and the absence of ν (OH) and its signal in ¹H-NMR are in favor to suggest the keto structure. The proposed structure is further suggested by the presence of weak bands located at 2913, 2818 and 2803 cm⁻¹ due to ν (C-H) of methyl and methylene groups, respectively. While, the CH deformation of CH₂ and CH₃ appeared in a strong feature at 1405 and 1356 cm⁻¹, respectively. The above arguments confirmed the acetyl hydrazine moiety. The δ NH bands may also including the ν C=C and ν C=N of rings.

The elemental analyses (Table 1), infrared and ¹H-NMR, ¹³C-NMR data and mass spectra are compatible with the structure of ligand as shown in Scheme 1.



Scheme 1 preparation of N-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide (HL)

Table (2) Infrared spectral bands and their assignments for ligand.

Band	Assignment
3287 (s)	ν NH ₂ (asym)
3124 (s)	ν NH ₂ (sym)
3045 (s)	ν NH (amide)
2913 (m), 2818 (m)	ν CH (CH ₃)
2803 (w)	ν CH (CH ₂)
1642 (w)	ν C=O
1577 (m)	δ NH ₂ + (ν C=C) ring
1505 (m)	δ NH amide+ (ν C=N) ring
1405 (s)	CH ₂ deformation
1356 (m)	CH ₃ deformation
1297 (m), 1222 (s)	ν C-N amide
1161	CH ₃ wagging
1109 (m), 1038 (s)	CH ₂ wagging + ν C-NH ₂
972 (s), 925 (m)	ν N-N
830 (s)	γ NH ₂
743 (s)	γ NH amide
590 (w)	δ C=O
520 (s)	Ring bending out plane + γ C=O
470 (s)	ρ NH ₂ amide

The infrared spectra bands and their assignments of ligand and its metal complexes listed in Tables (3) and shown in Fig. 1a-1h. The chemical structure of ligand, which was prepared as in Scheme 1) shows that the ligand could be considered as bidentate one via carbonyl oxygen atom (ketonic or enolic) and nitrogen atom of amino of hydrazine chain. The data obtained from IR spectra reveal that the spectra of all metal complexes display carbonyl stretching bands in range 1657-1661 cm⁻¹, indicating that the ligand reacts with metal ion in keto neutral form.

Table (3) Infrared spectral bands and their assignments for ligand and its metal complexes.

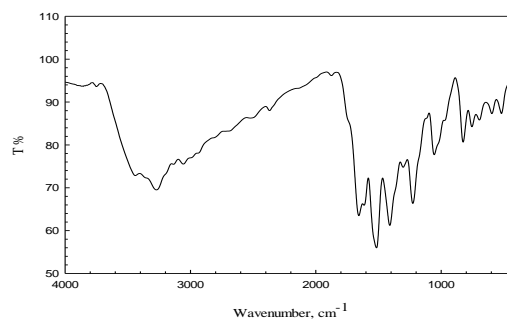
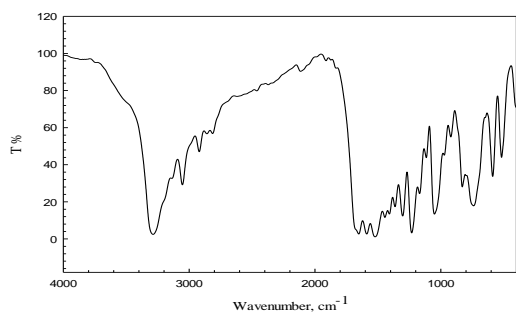
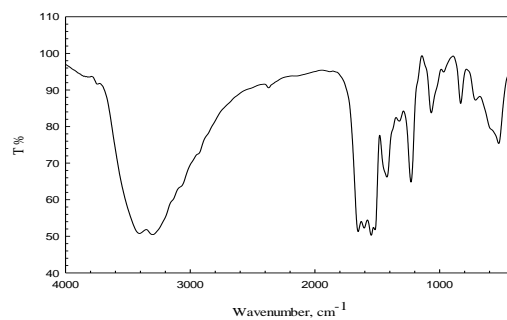
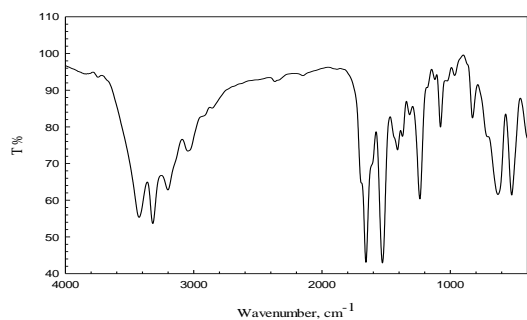
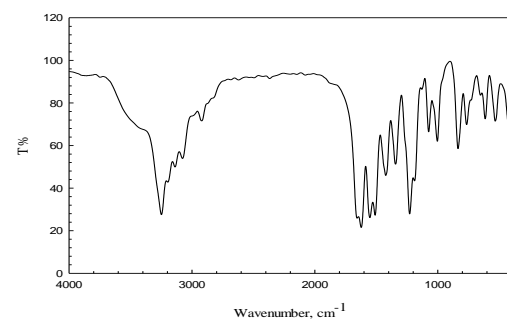
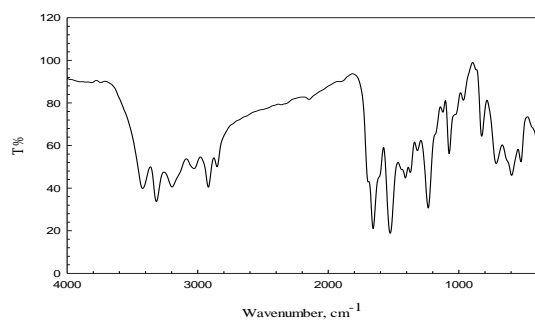
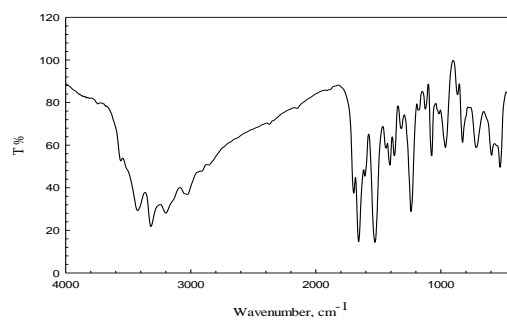
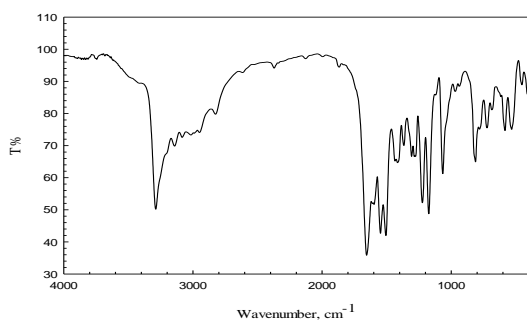
N o.	Compound	ν H ₂ O	ν NH ₂ (asym)	ν NH ₂ (sym), γ (NH ₂)	ν NH amide, γ (NH)	ν (C=O)	δ (NH ₂)	ν (N-N)	δ (C=O), γ (C=O) + ring bending	ν M-O	ρ NH ₂ , ν (M-N)
HL	C ₁₀ H ₁₃ N ₃ O ₃	-	3287(s)	3124(s) 830(s)	3045(s) 743(s)	1642(s)	1577 (s)	972(s) 925(m)	743(w), 590(s)	-	-
1	[(HL) ₂ CuCl ₂].6.5EtOH.1.5H ₂ O C ₃₃ H ₆₈ N ₆ O ₁₄ CuCl ₂	3450(w) 922(w)	3360(w), 3275(w)	3135(m) 831(v.w)	3060(b.m) 694(v.w)	1657(m)	1519(b .m)	1051(m) 965(w)	754(w) 686(v.w)	560(v. w)	453(w)
2	[(HL) ₂ Mn ₃ Cl ₆].3.5EtOH.3H ₂ O C ₂₇ H ₄₇ N ₆ O _{12.5} Mn ₃ Cl ₆	3435(sh) 1600(v.m)	3318(s)	3200, 853(w)	3048(w) 686(v.w)	1661(s)	1535(m)	1075(w) 971(w)	777(sh), 678(w)	550(w)	466(w)
3	[(HL)CrCl ₃ (H ₂ O)].3EtOH.3H ₂ O C ₁₆ H ₃₉ N ₃ O ₁₀ CrCl ₃	3422(w) 1608(sh.w)	3310(m)	3131(w) 847(v.w)	3067(w) 749(v.w)	1657(w)	1550(w)	1029(sh) 971(w)	724(sh)	585(m)	482(sh.w)
4	[(HL) ₃ Fe ₂ Cl ₄].Cl ₂ .7EtOH C ₄₄ H ₈₁ N ₉ O ₁₆ Fe ₂ Cl ₆	920(sh)	3428(w) 3320(m)	3196(w) 850(w)	3048(w) 722(v.w)	1657(s)	1531(s)	1075(w) 968(w)	716(w)	594(w)	506(w)
5	[(HL)ZnCl ₂].0.5EtOH.0.25H ₂ O C ₁₁ H _{16.5} N ₃ O _{3.75} ZnCl ₂	3428(b)	3255(m), 3200(sh. w)	3197(m) 871(v.m)	3078(w)	1657(w)	1554(m)	1075(w) 998(w)	767(m), 716(sh)	537(m)	430(m)
6	[(HL) ₂ CoCl ₂].2H ₂ O C ₂₀ H ₃₀ N ₆ O ₈ CoCl ₂	3558(sh) 918(w)	3425(w), 3291(m)	3147(w), 868(w)	3086(w)	1661(s)	1554(m)	1021(sh) 960(m)	762(sh), 716(m)	589(m)	488(w)
7	[(HL) ₂ VO]. SO ₄ C ₂₀ H ₂₆ N ₆ O ₁₀ SV	915(sh)	3428(m), 3324(m)	3200(w), 838(w)	3040(w)	1661(s)	1528(s)	1029(sh) 964(m)	770(sh)	525(m)	453(m)

Abbreviations: *v*: very, *s*: strong, *m*: medium, *w*: weak, *b*: broad, *sh*: shoulder.

The spectra of all complexes show that the ν (C=O) and γ (C=O) undergo positive shift by 15-20 cm⁻¹ in a weak feature relative that of free ligand. This suggests that the oxygen atom of carbonyl group takes place in coordination. This is also supported by the appearance of bands in range 594- 525 cm⁻¹, assignable to ν (M-O) [21, 22].

The spectra of complexes exhibit notable changes in different modes of vibrations namely (ν , δ , γ) of NH₂ and NH (amide) groups. The strong ν NH₂ (sym) and γ NH₂ ligand bands at (3124 and 830 cm⁻¹) are shifted to higher value by 7-76 cm⁻¹ and accompanied with weak appearance at complexation, to identify the M-N interaction [23]. Also, the bands characteristic of NH and γ NH of amide group of ligand reveal blue/red and red shift by 3-41 cm⁻¹ and blue shift by 21-49 cm⁻¹, respectively in complexes. This confirmed the terminal amino group of hydrazine is involvement in chelation. The positive shift in ν (N-N) at 972, 925 cm⁻¹ in free ligand by 57-103 cm⁻¹ in all metal complexes is further evidence for the bonding involving terminal hydrazine nitrogen atom[19]. The ρ NH₂ ligand band at 470 cm⁻¹ are shifted in complexes to 453-506 cm⁻¹ this shift verified ν (M-N)[22].

The spectra of complexes show bands in range 3450–3420 cm⁻¹ assigned ν (OH) of hydrated lattice water, whereas, the bands at 1610 and 915–922 cm⁻¹ are due to bending and rocking of coordinated water[24].


a) N-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide (HL)
b) [(HL)₂CuCl₂]·6.5EtOH·1.5H₂O

c) [(HL)₂Mn₃Cl₆]·3.5EtOH·3H₂O
d) [(HL)CrCl₃(H₂O)]·3EtOH·3H₂O

e) [(HL)₃Fe₂Cl₄]·Cl₂·7EtOH
f) [(HL)ZnCl₂]·0.5EtOH·0.25H₂O

g) [(HL)₂CoCl₂]·2H₂O
h) [(HL)₂VO]·SO₄
Fig.1 IR spectra of ligand (a) and its metal complexes (b-h)

Electronic absorption spectra and magnetic moments

Table (4) and Fig. 2 represented to the electronic absorption spectral data of the investigated metal complexes in nujol mull and their room temperature magnetic moments values (μ_{eff} . B.M.) per metal ion. Electronic spectrum of ligand displayed four electronic bands at 254, 293, 354, 446 nm. The first and the second electronic bands correspond to π - π^* transitions of the benzenoid system of the compounds [25,26]. The third and the fourth bands correspond to n - π^* transition due to the lone pairs of electrons on the nitrogen and oxygen atom [25].

The copper complex shows two fundamental bands at 662 and 421 nm in a broad and strong nature assigned to ${}^2B_{1g} \rightarrow {}^2B_{2g}$ and ${}^2B_{1g} \rightarrow {}^2E_g$ transitions, respectively, in distorted octahedral geometry [27,28]. The effected magnetic moment value of copper complex is 2.10 B.M. The value of magnetic moment is higher than the normal value (1.73 BM.) of the copper(II) complexes. This may be due to the spin-orbital coupling [25].

The electronic spectrum of trinuclear manganese complex $[(HL)_2Mn_3Cl_6] \cdot 3.5EtOH \cdot 3H_2O$ displays broad and weak bands at 718 and 575 nm assigned to ${}^6A_{1g} \rightarrow {}^4T_{1g} ({}^4G)$ and ${}^6A_{1g} \rightarrow {}^4E_g ({}^4D)$ transitions, respectively, consistent with octahedral structure [21].

The chromium complex show electronic spectral bands at 730 and 573 nm the bands correspond to the ${}^4B_{1g} \rightarrow {}^4E_g ({}^4T_{2g})$, ${}^4B_{1g} \rightarrow {}^4B_{2g} ({}^4T_{2g})$ transitions, respectively, gathered with magnetic moment values (3.89 B.M.) to assign a high spin octahedral structure [29].

The electronic spectrum of binuclear iron complex $[(HL)_3(FeCl_3)_2] \cdot 7EtOH$ displays bands at 725 and 531 nm corresponding to ${}^6A_{1g} \rightarrow {}^4T_{2g}$ and ${}^6A_{1g} \rightarrow {}^4A_{1g} (G)$ transitions, respectively, of octahedral geometry around Fe(III). The magnetic moment value (5.58 BM) of complex is consistent with high spin d^5 configuration in an octahedral field [30]. The low magnetic moment values of polynuclear complexes of Mn(II) or Fe(III) is 3.02 or 5.58 B.M. respectively, this is attributed to existence of magnetic interaction between Mn(II) or Fe(III) atoms and ligand bridges.

Since the zinc ion has a d^{10} configuration, the absorption at 379 nm could be referred to a charge-transfer transition. However, taking into account the spectrum and the configuration of the zinc(II) ion, a tetrahedral geometry may be assumed for its complex. [31,32]

The cobalt complex shows electronic spectral bands at 477 and 357 nm corresponding to (${}^4T_{1g} \rightarrow {}^4A_{2g}$) and (${}^4T_{1g} \rightarrow {}^4T_{2g}$) [33]. This absorption bands consistent with approximately octahedral cobalt(II). The magnetic moment value of Co(II) complex (4.5 B.M.) is consistent with the high spin octahedral geometry [34].

Although three (or four) d-d bands can be expected to appear in the spectrum of the $V^{IV}O$ complex in the visible region, they are often overlapping or obscured by strong LMCT (ligand-to-metal charge-transfer) bands. The spectra of complex shows broad bands in the range 500–600 nm (band II: $d_{xy} \rightarrow d_{x^2-y^2}$) and a shoulder at 600–710 nm (band I: $d_{xy} \rightarrow d_{xz}$, d_{yz}) [35]. Band III ($d_{xy} \rightarrow d_{z^2}$) occurs at 436 nm and is under much stronger LMCT bands.

All complexes exhibit electronic spectral bands at range 370 – 340 nm assigned to intra-ligand charge transfer.

The molar conductivity measurements for all metal complexes in (1×10^{-3} M) DMF solution at 25° C are found to be zero value indicates its non-electrolytic nature except for vanadyl complex is $116 \Omega^{-1} \text{ mol}^{-1}$ indicating their 1:1 electrolytic nature (Table 1). Also, the molar conductance value for ferric complex are found to be $120 \Omega^{-1} \text{ mol}^{-1}$ indicating the 2:1 electrolytic nature of these complexes [36].

Table (4) Nujol mull electronic spectral data (nm) and room temperature magnetic moments ($\mu_{\text{eff.}}$ /metal ion B.M.) for the metal complexes.

No.	Compounds	$\lambda_{\text{max.}}$ (nm)	$\mu_{\text{eff.}}$ / M, B.M.
HL	$\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}_3$	254 (m), 293(m), 354(w), 446(b)	-
1	$[(\text{HL})_2\text{CuCl}_2] \cdot 6.5\text{EtOH} \cdot 1.5\text{H}_2\text{O}$	258(m), 308(m), 359(m), 421(v.s), 662(b)	2.22
2	$[(\text{HL})_2(\text{MnCl}_2)_3] \cdot 3.5\text{EtOH} \cdot 3\text{H}_2\text{O}$	254(m), 313(w), 354(b), 575(v.w), 718(sh)	3.02
3	$[(\text{HL})\text{CrCl}_3(\text{H}_2\text{O})] \cdot 3\text{EtOH} \cdot 3\text{H}_2\text{O}$	262(m), 313(m), 356(w), 432(s), 573(b), 730(sh)	3.89
4	$[(\text{HL})_3\text{Fe}_2\text{Cl}_2] \cdot 2\text{Cl}_2 \cdot 7\text{EtOH}$	258(m), 308(w), 357(w), 483(sh), 531(b), 725(sh)	5.58
5	$[(\text{HL})\text{ZnCl}_2] \cdot 0.5\text{EtOH} \cdot 0.25\text{H}_2\text{O}$	259(m), 300(w), 357(m), 379(w)	0
6	$[(\text{HL})_2\text{CoCl}_2] \cdot 2\text{H}_2\text{O}$	258(m), 298(m), 357(w), 477(b)	4.5
7	$[(\text{HL})_2\text{VO}] \cdot \text{SO}_4$	257(m), 304(w), 362(sh), 436(s)	1.7

Abbreviations: v: very, s: strong, m: medium, w: weak, b: broad, sh: shoulder.

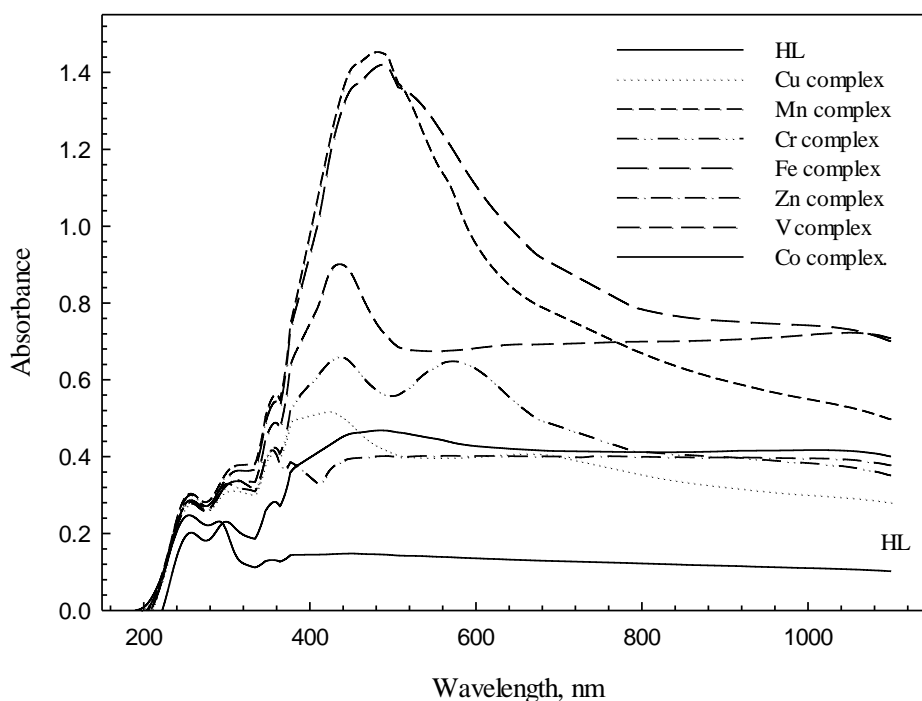


Fig. 2 Electronic absorption spectra of ligand and its metal complexes.

Thermal analysis of metal complexes

Thermogravimetric measurements were undertaken to assigned the nature of solvent and the data characterized the thermal decomposition behaviors of complexes are presented in Table (5). Thermal degradation of complexes were studied within the temperature range of 20-800°C

The thermogravimetric curves of compounds obtained for copper, manganese, chromium, iron and cobalt complexes show that a mass loss occurs within 20–270 °C range which corresponds to release the solvent of crystallization. This is characterized by DTG exothermic peaks as shown in Fig. 3.

The TGA curves show also, the thermal stability up to 200–270 °C. The complexes start to decomposition above this temperatures forming metal oxide as residue at 680–770 °C.

All complexes except zinc and vanadium complexes exhibit similar thermal decomposition, which take place mainly in three stages. The first stage occurs within the temperature range 20–270 °C corresponding to release the solvent of crystallization.

The second stage occurs in temperature range 114–572 °C represented by removal of coordinated chloride associated with partial decomposition of organic ligand.

The final third stage takes place in 270–770 °C range assigned to decomposition of rest organic ligands. Where, the decomposition processes take place under nitrogen with the formation of metal oxide except vanadium complex give VO, this indicates the ligand used as oxidizing agent.

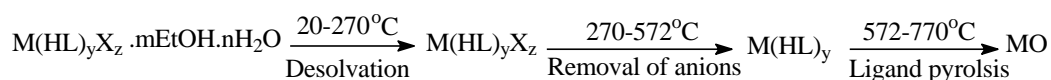
The DTG curves show all the decomposition processes characterized by exothermic reaction at T_{max} (315 °C), (125, 265, 350 °C), (194, 262, 405, 726 °C), (124, 258, 278, 409, 598 °C), (315, 347, 545 °C), (125, 230, 305, 362 °C), (279, 327 °C) for Cu, Mn, Cr, Fe, Zn, Co and V complexes respectively. The TGA data and their assignments are summarized in (Table 5).

Table 5 TGA data of metal complexes

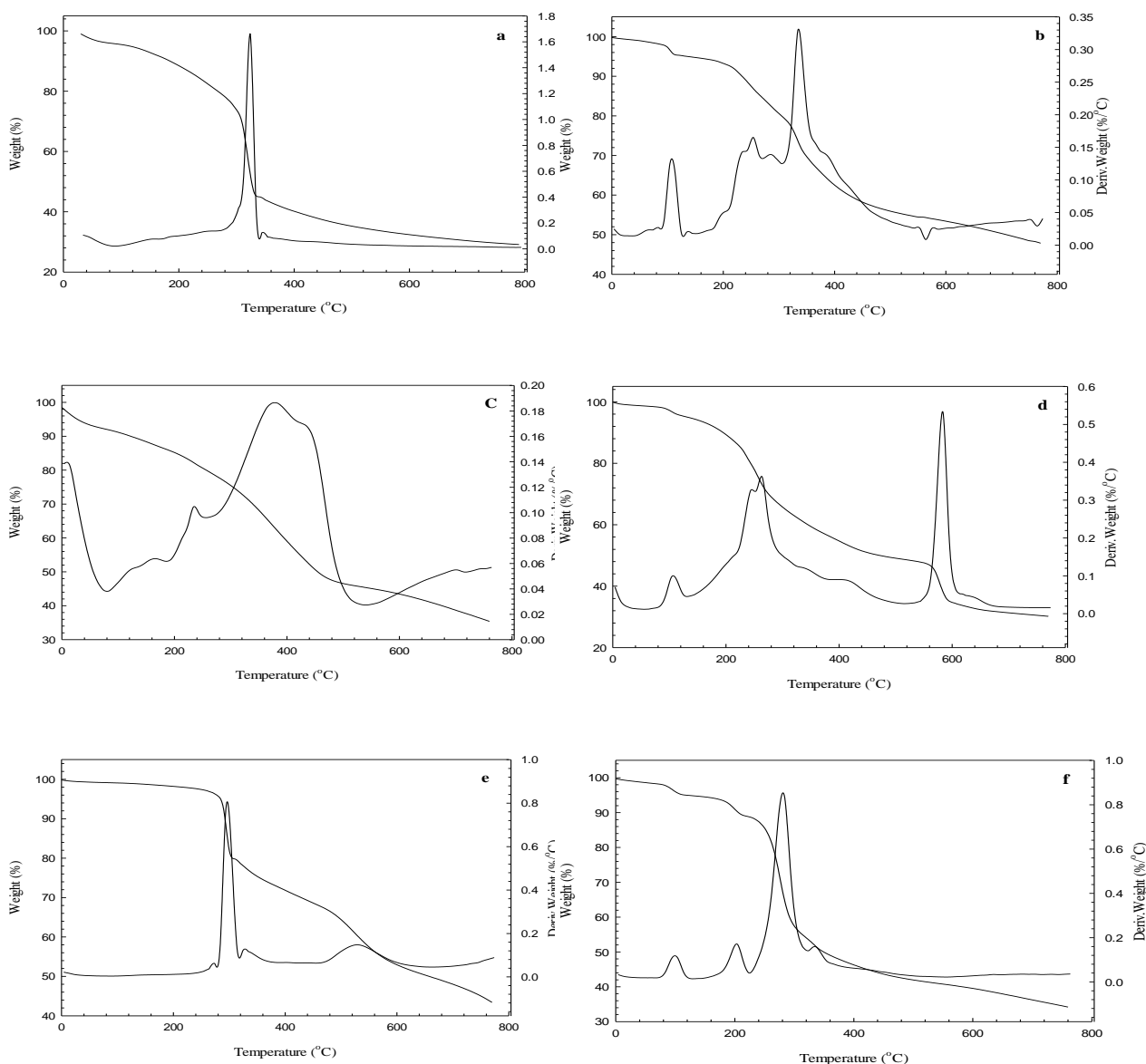
No.	Complex	Temperature Range (°C)	Weight loss Found/(Calcd.) %	Assignment	T _s (°C)
1	[(HL) ₂ CuCl ₂].6.5EtOH.1.5H ₂ O	30-99	2.964(2.9975)	Loss 1.5 molecules of hydrated water ^(a) s.d.	277
		99 – 270	18.12(17.74)	Loss 3.5 molecules of ethanol ^(d)	
		270 – 750	45.50(44.47)	Loss of 3 molecules of ethanol + Decomposition of organic ligand ^(d)	
		750	33.39(34.82)	4CuO ^(f)	
2	[(HL) ₂ Mn ₃ Cl ₆].3.5EtOH.3H ₂ O	25 – 168	5.294(5.19)	Loss 1.5 molecules of hydrated water ^(a) s.d.	340
		168 – 335	14.46(15.49)	Loss 3.5 molecules of ethanol ^(d)	
		335 – 758	32.63(31.39)	Decomposition of organic ligand ^(d)	
		758	47.62(47.79)	7MnO ^(f)	
3	[(HL)CrCl ₃ (H ₂ O)].3EtOH.3H ₂ O	22 – 114	7.926(7.60)	Loss 2.5 molecule of hydrated water ^(a) s.d.	355
		114 – 293	12.06(12.33)	Loss 0.5 molecules of hydrated water + Loss one molecule of coordinated water + loss one molecule of ethanol ^(d)	
		293 – 572	34.67(33.27)	Loss 3 molecules of coordinated chloride ions + loss 2 molecule of ethanol ^(d)	
		572 – 770	10.28(12.71)	Decomposition of organic ligand ^(d)	
		770	35.05(34.09)	1.33 Cr ₂ O ₃ ^(f)	
4	[(HL) ₃ Fe ₂ Cl ₄].Cl ₂ .7EtOH	20 – 272	20.85(20.97)	Loss 6 molecules of ethanol ^(a) s.d.	290
		272 – 425	24.56(25.20)	Loss one molecule of ethanol + loss 4 chloride ions + loss 2 coordinated chloride ions + loss 0.31 of ligand (CH ₂ CONHNH ₂) ^(d)	
		425 – 680	24.48(25.14)	Decomposition of rest of organic ligand ^(d)	
		680	30.09(32.75)	2.5 Fe ₂ O ₃ ^(f)	
5	[(HL)ZnCl ₂].0.5EtOH.0.25H ₂ O	20 – 335	20.82(19.49)	Loss 0.25 molecule of water + Loss 2 molecules of coordinated chloride ions ^(a) s.d.	365
		335 – 460	9.581(9.560)	Loss 0.5 molecule of coordinated ethanol + Loss CH ₂ ^(d)	
		460 – 770	26.67(28.89)	Decomposition of rest of organic ligand ^(d)	
		770	42.86(42.06)	2ZnO ^(f)	
6	[(HL) ₂ CoCl ₂].2H ₂ O	25 – 168	5.203(5.878)	Loss 2 molecules of hydrated water ^(a) s.d.	285
		168 – 260	5.865(5.789)	Loss one coordinated chloride ion ^(d)	
		260 – 350	34.73(34.66)	Loss one coordinated chloride ion + loss 0.73 of ligand + CH ₂ ^(d)	
		350 – 740	20.22(19.38)	Decomposition of rest of organic ligand ^(d)	
		740	33.97(34.29)	2CoO+5C ^(f)	
7	[(HL) ₂ VO].SO ₄	187– 290	16.17(16.12)	Loss of SO ₄ ion ^(a) s.d.	318
		290 – 400	71.55(72.61)	Decomposition of organic ligand ^(d)	
		760	12.15(11.27)	VO ^(f)	

Abbreviations: s.d.: start of decomposition, ^(a): dehydration, ^(d): decomposition, ^(f): final product, T_s: thermal stability.

The pathway of the decomposition mechanism of metal complexes may be proposed as follows:



TGA curves of zinc and vanadium complexes show three stages, the first one occurs within the temperature range 29–335 °C corresponding to release the solvent of crystallization. Once, removal the ethanol and water, the complex showed progressive decomposition within temperature range 335–460 °C assigned to decomposition of organic ligand. The decomposition reaction of zinc and vanadium complexes ended with the formation of ZnO and VO respectively.



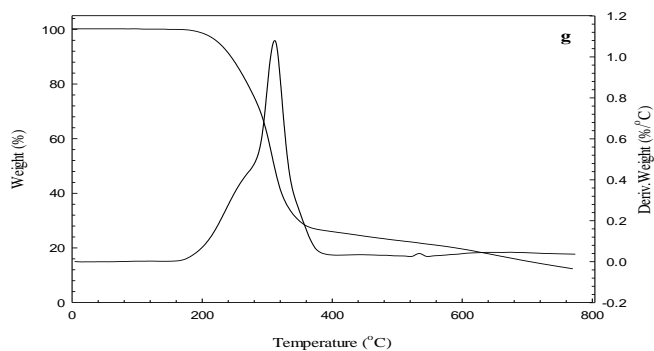
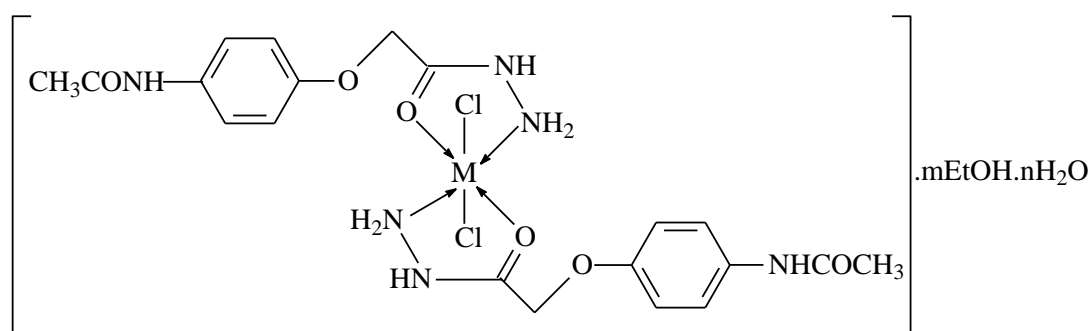
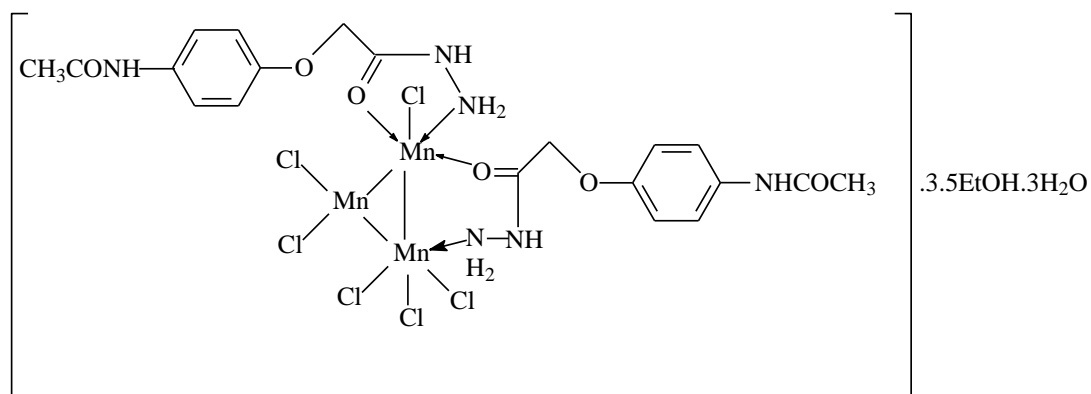


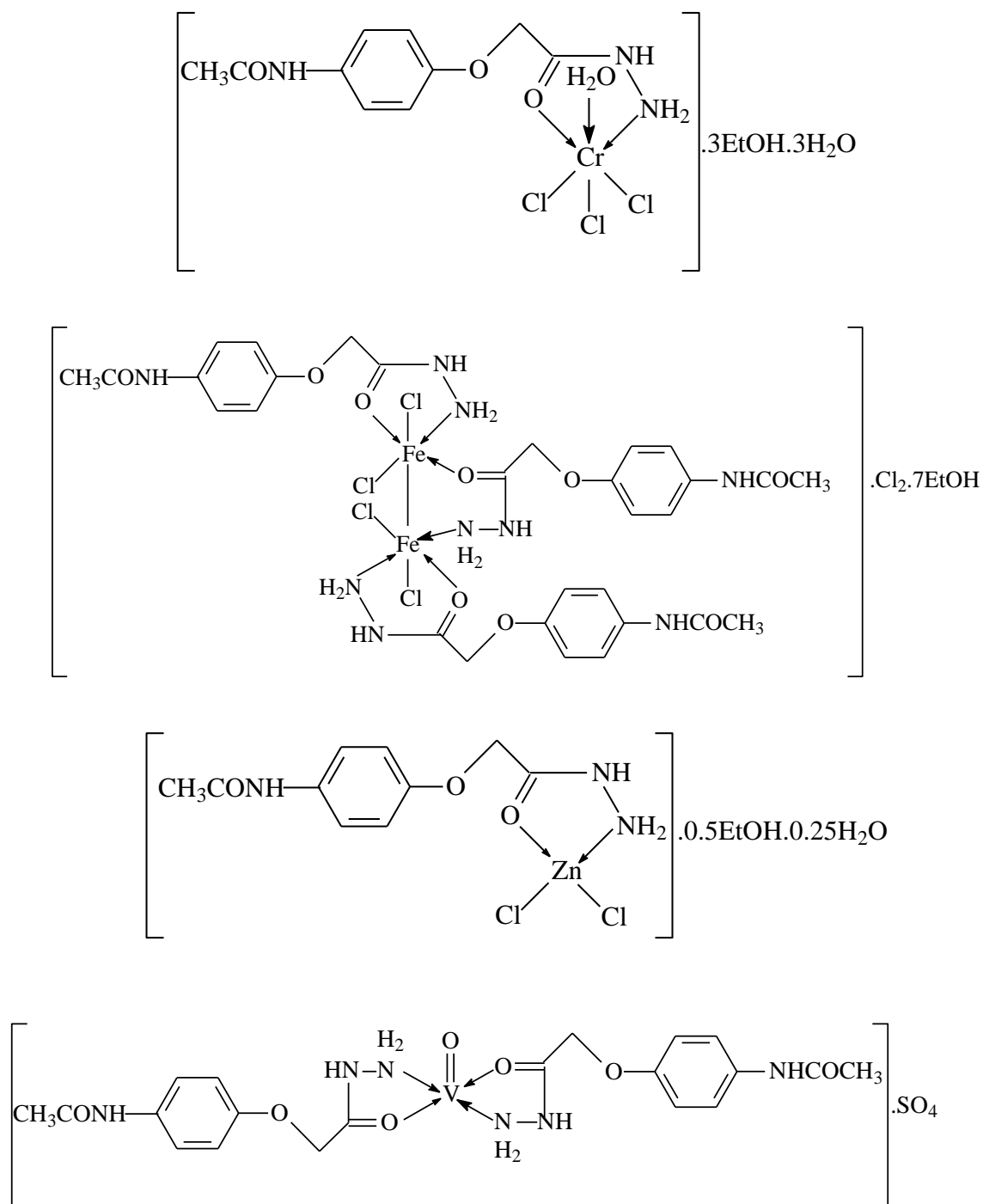
Fig. 3 TGA and DTG curves of metal complexes: a) $[(HL)_2CuCl_2] \cdot 6.5EtOH \cdot 1.5H_2O$, b) $[(HL)_2(MnCl_2)_3] \cdot 3.5EtOH \cdot 3H_2O$, c) $[(HL)CrCl_3] \cdot 3EtOH \cdot 4H_2O$, d) $[(HL)_3(FeCl_3)_2] \cdot 7EtOH$, e) $[(HL)ZnCl_2] \cdot 0.5EtOH \cdot 0.25H_2O$, f) $[(HL)_2CoCl_2] \cdot 2H_2O$, g) $[(HL)VO(SO_4)] \cdot 2EtOH$

The structure of metal complexes



M	m	n
Cu(II)	6.5	1.5
Co(II)	0	2





Microbiological investigation of compounds

Antibacterial screening of the complexes against *Escherichia coli* (Gram –ve, *E. coli*) and *Staphylococcus aureus* (Gram +ve, *S. aureus*) was investigated. The antibacterial activity of the compounds was evaluated according to size of inhibition zone formed around the well on the seeded agar plate.

The results show that *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide (HL) and its metal complexes were found to have varied degree of inhibitory effect against the both bacteria species. The highest activity was reported with (HL) and some of its complexes against *E. coli* and *S. aureus* (Figure 4).

Fig. 4 Zone of inhibition of *E. coli* and *S. aureus* for (HL) and zinc complex.

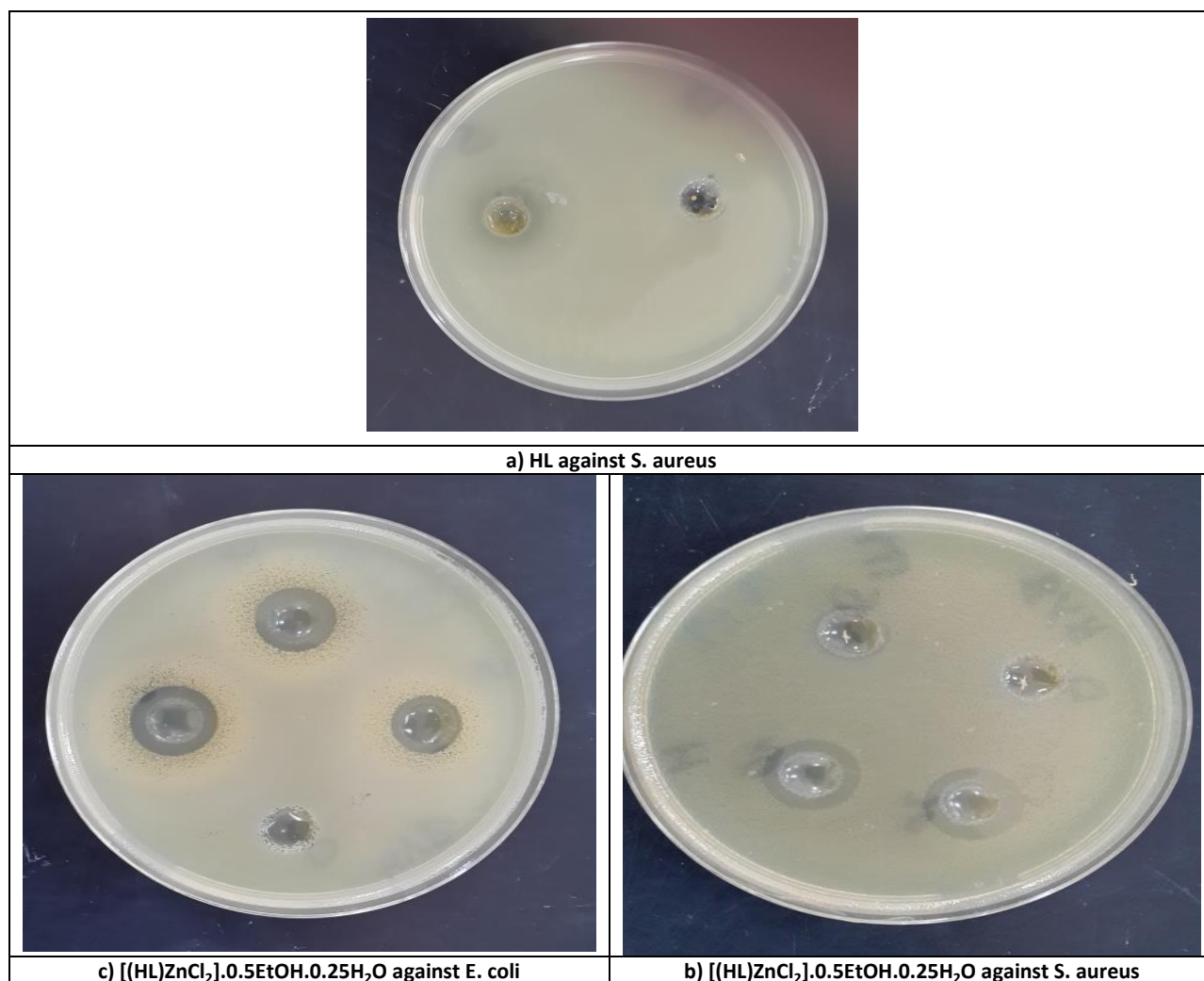


Fig. 4 Zone of inhibition of *E. coli* and *S. aureus* for (HL) and zinc complex.

Table 6 shows that (HL) have valuable inhibition activity ranged (28-35 mm) against *E. coli* which is more powerful than that of antibiotics (ampicillin 10 and tetracycline 30) but it have no activity against *S. aureus* at all concentrations. While the [(HL)₃Fe₂Cl₄].Cl₂.7EtOH complex possesses no activity against the both type of bacteria. The results are in agreement with the earlier report of their non-activity [37].

Table 6 Antibacterial activities of the ligand and its complexes showing the zone of inhibition against the organisms.

Ligand/ complexes	E. coli			S. aureus		
	Zone of inhibition (mm)					
	10 mg/mL	20 mg/mL	30 mg/mL	10 mg/mL	20 mg/mL	30 mg/mL
C ₁₀ H ₁₃ N ₃ O ₃	28	31	35	0	0	0
[(HL) ₂ CuCl ₂].6.5EtOH.1.5H ₂ O	15	19	34	0	0	0
[(HL) ₂ Mn ₃ Cl ₆].3.5EtOH.3H ₂ O	0	0	0	10	12	14
[(HL)CrCl ₃ (H ₂ O)].3EtOH.3H ₂ O	0	0	0	14	15	16
[(HL) ₃ Fe ₂ Cl ₄].Cl ₂ .7EtOH	0	0	0	0	0	0
[(HL)ZnCl ₂].0.5EtOH.0.25H ₂ O	14	15	17	12	16	19
[(HL) ₂ CoCl ₂].2H ₂ O	18	25	34	0	0	0
[(HL) ₂ VO].SO ₄	0	0	0	15	17	20
ampicillin 10	7.2			7.5		
tetracycline 30	22			22		

The results of antibacterial activities of both $[(HL)_2CuCl_2].6.5EtOH.1.5H_2O$ and $[(HL)_2CoCl_2].2H_2O$ complexes show that inhibitory zones range (15-34 mm) which indicates that they have higher antibacterial activities compared to both antibiotics and this effect increase with increasing concentration of complexes.

The data also suggest that the $[(HL)_2Mn_3Cl_6].3.5EtOH.3H_2O$, $[(HL)CrCl_3(H_2O)].3EtOH.3H_2O$ and $[(HL)_2VO].SO_4$ complexes were toxic against both the bacteria species. These complexes were found to have high activity (10-20 mm) than ampicillin 10 antibiotic (7.2 mm), but they have low activity than tetracycline 30 antibiotic (22 mm) against *E. coli*. Also these complexes possess no activity against *S. aureus*.

The $[(HL)ZnCl_2].0.5EtOH.0.25H_2O$ complex was the only complex which effected on both bacteria. The results of inhibition activity were found more powerful (14-17 mm) than that of ampicillin 10 antibiotic (7.2 mm), but they have low activity than tetracycline 30 antibiotic (22 mm) against *E. coli*. Also, the tested complexes were less active (12-19 mm) with reference to the standard antibiotic tetracycline 30 (22 mm) and were high active than ampicillin 10 antibiotic (7.5 mm) against *S. aureus* bacteria.

Zone of inhibition of the active samples of ligand and its metal complexes were increases with increasing concentration of the complexes. *N*-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)acetamide [HL], due to chelation which increases lipophilic character, favoring its permeation through lipid layers of the bacterial membrane as documented by [38].

CONCLUSION

N-(4-(2-hydrazinyl-2-oxoethoxy)phenyl)-acetamide (HL) is a very interesting ligand from point of view of its applications. In this paper, the synthesis and properties of the ligand and its complexes were investigated. The complexes with the empirical formulas: $[(HL)_2CuCl_2].6.5EtOH.1.5H_2O$, $[(HL)_2Mn_3Cl_6].3.5EtOH.3H_2O$, $[(HL)CrCl_3(H_2O)].3EtOH.3H_2O$, $[(HL)_3Fe_2Cl_4].Cl_2.7EtOH$, $[(HL)ZnCl_2].0.5EtOH.0.25H_2O$, $[(HL)_2CoCl_2].2H_2O$ and $[(HL)_2VO].SO_4$ were prepared. The structures of these complexes have been confirmed from the elemental analysis, FT-IR spectroscopy and thermal analysis. Thus, from the FTIR spectrum, it is concluded that (HL) behave as a bidentate ligand coordinated to the metal ion. The coordinated water was proved and determined by thermal analysis. The thermal investigation (studied by TG/DTG techniques) shows that obtained complex decomposes progressively, and the first step of thermolysis is dehydration. The final product of the thermal decomposition is metal oxides, which through its percentage confirms the empirical formulae of the new complexes prepared.

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