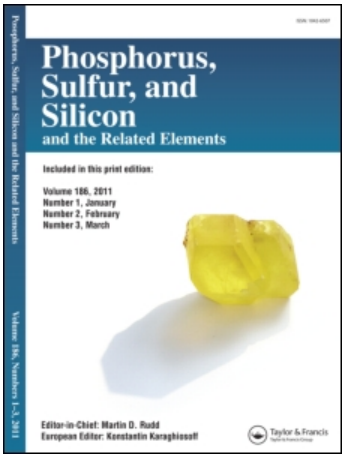

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Synthesis, Spectral, Characterization, and Anticancer Activity of Some Binary and Mixed Ligand Complexes of 4-Methyl-2-Pentanone Thiosemicarbazone and Some Amino Acids

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SYNTHESIS, SPECTRAL, CHARACTERIZATION, AND ANTICANCER ACTIVITY OF SOME BINARY AND MIXED LIGAND COMPLEXES OF 4-METHYL-2-PENTANONE THIOSEMICARBAZONE AND SOME AMINO ACIDS

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The Schiff base ligand 4-methyl-2-pentanone thiosemicarbazone (MPTSC) (HL) has been synthesized by the interaction of 4-methyl-2-pentanone (MP) and thiosemicarbazone (TSC). The Ni(II), Cu(II), and Fe(III) binary complexes of this ligand have been prepared. The ternary complexes of VO(IV) and Mn(II) ions with HL and glutamine (Glu) as a secondary ligand, in addition to VO(IV), Mn(II), and La(III) with HL and glycine (Gly) as a secondary ligand, have also been synthesized. The binary and ternary complexes have been characterized based on elemental analysis, IR, UV-VIS, molar conductance, mass spectra, magnetic moment, and ESR measurements. The magnetic moment, UV, and ESR studies suggest that Ni(II) and Cu(II) complexes are square planar, whereas Fe(III), Mn(II), and La(III) complexes have octahedral geometry, but VO(IV) ternary complexes have square pyramidal geometry. The analytical data indicate that the metal-to-ligand ratio in binary complexes is 1:1, except HL-Cu(II) chloride complex where the metal-to-ligand to secondary ligand ratio in ternary complexes is 1:1:1. The anticancer studies showed that the anticancer activity is in the decreasing order: ternary complexes > binary complexes > free ligand (HL).

Supplemental materials are available for this article. Go to the publisher's online edition of* Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.

Keywords Amino acids; mixed ligands; thiosemicarbazone

INTRODUCTION

In recent decades, considerable studies have been carried out on the interaction between various metal ions and ligands that takes place in biochemical processes.[1] The biological importance of mixed ligand complexes is that they are sometimes more effective than the free ligands.[2] Also, amino acids and their compounds with different metal ions play an important role in biology, pharmacy, and industry. Moreover, coordination chemists have been interested for many years in the donor properties of amino acids as models for metal–protein interaction, and recent studies have also emphasized the reactivity of

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coordinated amino acid in the hope of finding simple and easily interpretable models for the reactivity of some biological systems that contain metals. Furthermore, a great deal of attention has been paid recently to the close relationships between metals, or their complexes, and carcinogenesis, and some metal complexes are used in anticancer therapy. In cancer chemotherapy, amino acids assume a remarkable importance,[3] and when discussing the possibility of introducing an amino acid into an anticancer drug, it is very important to know whether the amino acid forms metal complexes, and in particular, any special metal complexes. Furthermore, thiosemicarbazones and their complexes[4–6] have received considerable attention because of their potential therapeutic activities against bacterial and viral infections,[7,8] tuberculosis, [9] and leprosy.[10] In addition, particular attention has been given to their antitumor activity, which seems to be due to inhibition of DNA synthesis caused by a modification in the reductive conversion of ribonucleotides to deoxyribonucleotides.[11] The interaction of metal complexes with DNA is an area of intense interest to both inorganic chemists and biochemists.[12] On the other hand, the importance of metal compounds in medicine dates back to the 16th century with reports on the therapeutic use of metals or metal-containing compounds in the treatment of cancer. Metal ions are electron-deficient, whereas most biological molecules (proteins and DNA) are electron rich; consequently, there is a general tendency for metal ions to bind to and interact with many important biological molecules. Metal ions also have a high affinity for many small molecules, e.g., O_2, that are crucial to life. These considerations alone have fueled much of the past and current interest in developing novel means to use metals or metal-containing agents to modulate biological systems.[13]

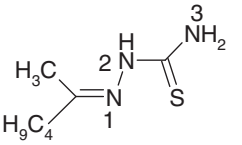
Moreover, the coordination chemistry of vanadium is of great current interest because of the discovery of its presence in abiotic as well as biotic systems. Another important impetus to the coordination chemistry of vanadium in the context of medical applications has arisen from ability of vanadium complexes to promote the insulin mimetic activity pathophysiological state of diabetes mellitus in humans.[14] Nickel species in various coordination environments are also of interest to inorganic biochemists. For instance, some nickel complexes of thiosemicarbazone derivatives are observed to exhibit antitumor activity.[15]

Also, Cu(II), La(III), and Mn(II) complexes have found possible medical uses in the treatment of many diseases including cancer.[16–18]

The first row transition metal ions occupy an important position due to the involvement of these elements in various biological systems.[18] Furthermore, some lanthanum complexes possibly represent a new class of potential antitumor agent.[17]

RESULTS AND DISCUSSION

The structure of the ligand is shown in Figure 1. The quantities used are shown in Table I. The elemental and physical data of the ligand HL and its complexes (Table II)



(HL)

Figure 1 Structure of the ligand.

Table I Amounts of the reactants used in the formation of the metal complexes

No.	Complex	Metal salt	Metal chloride or acetate in ethanol (10–20 mL)		Ligand HL in ethanol (15 mL)		Glu or Gly in ethanol (10 mL)		Sodium hydroxide	
			Mass (g)	Mmol	Mass (g)	Mmol	Mass (g)	Mmol	Mass (g)	Mmol
1	$[Ni(HL)Cl_2].H_2O$	$NiCl_2.6H_2O$	0.247	2.0	0.346	2.0				
2	$[Cu(HL)_2]Cl_2.4H_2O$	$CuCl_2.2H_2O$	0.340	2.0	0.692	4.0				
3	$[Cu(HL)(OH_2)_2](CH_3COO)_2{\cdot}H_2O$	$Cu(Ac)_2$	0.364	2.0	0.346	2.0				
4	$[Fe(HL)Cl_2{\cdot}H_2O]$	$FeCl_26H_2O$	0.540	2.0	0.346	2.0				
5	$[VO(Glu)(L)].5H_2O$	$VOSO_4.H_2O$	0.360	2.0	0.346	2.0	0.292	2.0	0.16	4.0
6	$[Mn(Glu)(L)].H_2O$	$MnCl_2.2H_2O$	0.322	2.0	0.346	2.0	0.292	2.0	0.16	4.0
7	$[VO(Gly)(HL)].4H_2O$	$VOSO_4.H_2O$	0.360	2.0	0.346	2.0	0.150	2.0	0.16	4.0
8	$[Mn(Gly)(HL)]Cl.2H_2O$	$MnCl_2.2H_2O$	0.322	2.0	0.346	2.0	0.150	2.0	0.16	4.0
9	$[La(Gly)(HL)Cl_2].H_2O$	$LaCl_3.7H_2O$	0.500	2.0	0.346	2.0	0.150	2.0	0.16	4.0

show that the stoichiometry of the complexes obtained is 1:1, 1:2 (metal:ligand), and 1:1:1 (ligand:metal:AA).

Mass Spectra of Ligand HL and Its Complexes

The mass spectra of the free ligand HL and its binary and ternary complexes **1–9** exhibit the molecular ion peaks at *m/e* 173, 322, 554, 409, 354, 475, 391, 385, 408, and 476, respectively, which confirm their proposed formulae. Their proposed pathway fragmentation patterns are provided as supplemental files (Figures S1 and S2, respectively, Supplemental Materials, available online).

IR Spectra

The main bands of the HL ligand and its complexes are summarized in Table S1 (Supplemental Materials). The spectrum of the free ligand HL shows bands at 1607, 1597, and 853 cm^{-1}, characteristic of δ NH_2, υ C=N, and υ C=S groups, respectively. Also, the absence of the υ S−H band, suspected at about 2570 cm^{-1}, indicates the thionic nature of the ligand. The appearance of the δ NH at 3160 cm^{-1} gives further support for the existence of the ligand in the thione form.

Moreover, the δ NH_2 band of the ligand (1607 cm^{-1}) remains at the same position, 1600–1610 cm^{-1}, in all binary and ternary complexes, indicating that the NH_2 group does not participate in coordination in these complexes.[19]

The band of the azomethine group of the ligand at 1597 cm^{-1} shifts to higher or lower frequencies[20] in all binary and ternary complexes (1570–1647 cm^{-1}). This band appears as a broad one centered at 1612 cm^{-1} in the iron complex, suggesting coordination of the azomethine nitrogen to the metal atom.[20] Furthermore, the υ C=S vibration in the free ligand is either shifted or absent in all binary and ternary complexes, indicating the involvement of a sulfur atom in coordination.[21]

Table II Analytical and physical data of the ligand HL with its binary and ternary complexes

Compounds	FW	M:L L:M:L	Yield %	Color	Mp (°C)	Analysis% Found (Calcd.) %C	%H	%N	%S	Molar conductance Λ_m (Ω^{-1} cm^2 mol^{-1})
HL $C_7H_{15}N_3S$	173.28		92	White	209–211	48.44 (48.52)	8.76 (8.72)	24.28 (24.25)	18.67 (18.50)	
Binary complexes										
$[Ni(HL)Cl_2].H_2O$ (**1**)	320.89	1:1	85	Green	320–322	26.25	(5.42)	13.11	9.88	15.32
$C_7H_{17}Cl_2N_3OSNi$						(26.20)	(5.34)	(13.09)	(10.00)	
$[Cu(HL)_2]Cl_2.4H_2O$ (**2**)	553.06	1:2	55	Brown	289–295	30.45	6.85	15.35	11.45	69.10
$C_{14}H_{38}Cl_2N_6O_4S_2Cu$						(30.40)	(6.93)	(15.20)	(11.59)	
$[Cu(HL)(OH_2)_2](CH_3COO)_2{\cdot}H_2O$ (**3**)	408.96	1:1	45	Brown	329–337	32.25	6.58	10.30	7.79	87.42
$C_{11}H_{27}N_3O_7SCu$						(32.31)	(6.65)	(10.27)	(7.84)	
$[Fe(HL)Cl_2{\cdot}H_2O]$ (**4**)	353.5	1:1	60	Brown	298–304	23.66	4.73	11.80	9.11	12.34
$C_7H_{17}Cl_3N_3OSFe$						(23.78)	(4.85)	(11.89)	(9.07)	
Ternary complexes										
$[VO(Glu)(L)].5H_2O$ (**5**)	475.43	1:1:1	90	Green	340–350	30.41	7.31	14.68	6.67	8.91
$C_{12}H_{34}N_5O_9SV$						(30.32)	(7.21)	(14.73)	(6.74)	
$[Mn(Glu)(L)].H_2O$ (**6**)	391.37	1:1:1	75	Brown	340–345	36.61	6.55	17.74	8.30	23.39
$C_{12}H_{26}N_5O_4SMn$						(36.83)	(6.70)	(17.89)	(8.19)	
$[VO(Gly)(HL)].4H_2O$ (**7**)	385.33	1:1:1	89	Green	345–354	28.19	6.78	14.59	8.29	31.52
$C_9H_{26}N_4O_7SV$						(28.05)	(6.80)	(14.54)	(8.32)	
$[Mn(Gly)(HL)]Cl.2H_2O$ (**8**)	409.79	1:1:1	51	Brown	340–350	36.42	6.77	13.62	7.73	52.91
$C_9H_{27}Cl\ N_4O_6SMn$						(36.38)	(6.64)	(13.67)	(7.82)	
$[La(Gly)(HL)Cl_2].H_2O$ (**9**)	475.16	1:1:1	83	White	330–345	22.82	4.54	11.66	6.81	16.22
$C_9H_{21}Cl_2N_4O_3SLa$						(22.75)	(4.45)	(11.79)	(6.75)	

Coordination of the azomethine N to the metal ion is also suggested by occurrence of the N–N band at higher wave numbers in all the studied complexes.[22] These results indicate the coordination of the thiosemicarbzone ligand to all metal ions in binary and ternary complexes through the N azomethine and sulfur atoms as bidentate chelating agents.

On the other hand, it was found that many complexes of the metal–amino acid ligands act as bidentate chelating agents that coordinate through the amino and carboxyl groups.[23] A few cases are known in which the two carboxyl oxygens are bound to the metal in a bidentate mode, leaving the amino group free, and this behavior takes place in the presence of a bulky organic group bound to the metal.[24]

Also, the spectra of complex **3** showed the appearance of two characteristic bands at 1525 and 1367 cm^{-1}, attributed to *asym*(OCO) and *sym*(OCO), respectively, having the separation value Δ(OCO) 158 cm^{-1}, suggesting the ionic nature of the acetate.[25]

Combination and overtone bands in the 2042–2110 cm^{-1} region of Glu and Gly amino acids, characteristic of NH_3^+ groups, are absent in the spectra of all ternary complexes, except complex **5** where this band remains at the same position (2042 cm^{-1}), indicating coordination of the NH_2 group in these complexes.[26] Furthermore, the C=O amide band of the free Glu at 1686 cm^{-1} is unchanged in complexes **5** and **6**, excluding participation of the amide C=O group in complexation. In addition, there are differences in the positions of asym(OCO) and sym(OCO) stretching vibrations of the free amino acids and the complexes consistent with the coordination of the carboxyl groups.

The $\Delta\upsilon$(OCO) values for all the complexes except complex **5** are greater than the $\Delta\upsilon$(OCO) values found for the free amino acids. Such increase in the value of $\Delta\upsilon$(OCO) is indicative of monodentate coordination of the amino acid via the carboxyl group.[25] In the case of complex **5**, the $\Delta\upsilon$(OCO) becomes smaller as compared to that in the free Glu acid, showing the bidentate chelation of the carboxylate group in this complex.[25]

^{1}H NMR Spectra

The ^{1}H NMR spectra of the free ligand HL in chloroform solution with assignments are reported in the Experimental section. The hydrazinic proton (-N^2H) of the free ligand (HL) appears as a single broad peak at δ 8.56 ppm. The free thiosemicarbazone ligand showed a singlet at δ 6.45 ppm assigned to the amino (N^3H_2) protons. Unfortunately, the diamagnetic binary nickel complex **1** is insufficiently soluble in chloroform or in DMSO to acquire a ^{1}H NMR spectrum.

Magnetic, Electronic, and ESR Spectral Studies

The electronic spectra of the free ligand HL show three bands, 275, 290, and 310 nm, assigned to $\pi \rightarrow \pi^*$ and n$\rightarrow \pi^*$ in the free ligand,[15] whereas the bands in the range 210–320 nm in the spectra of the amino acids can be assigned to n$\rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ intraligand transitions associated to amino acids.[27] The electronic spectra of HL and its complexes and magnetic moment are shown in Table S2 and Figure S3 (Supplemental Materials).

Structures of the Binary Complexes

The room temperature magnetic susceptibility data of the HL-Ni (II) complex shows that this complex is diamagnetic and of low-spin with $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1E_g$ transitions,

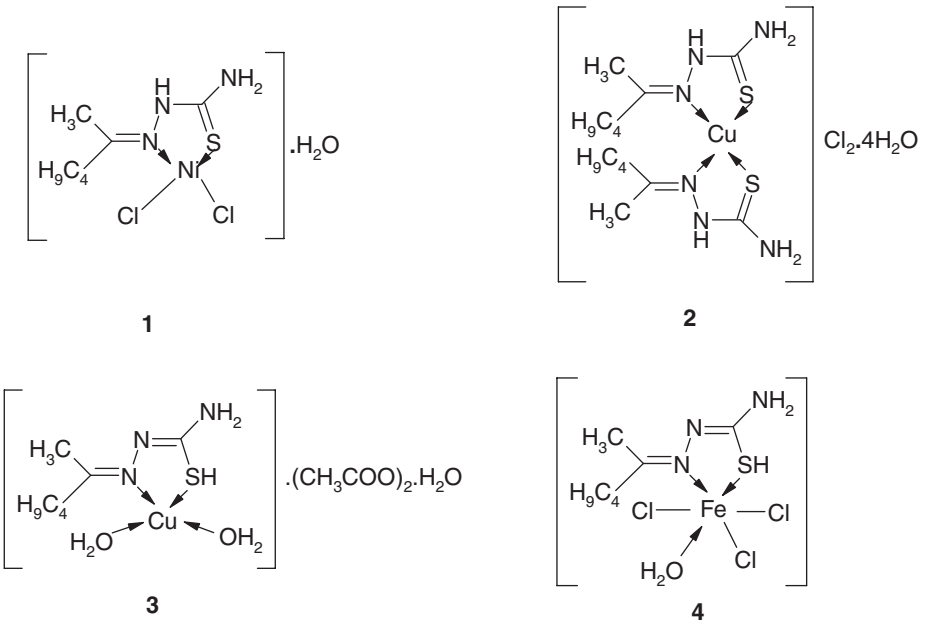


Figure 2 Structure of binary complexes **1–4**.

respectively.[23] This complex is of square-planar geometry because it is diamagnetic and there is no band seen below 1000 nm.[28]

The two Cu complexes have a magnetic moment value of 1.80 and 1.88 BM, respectively, corresponding to the presence of one unpaired electron.[29]

The spectrum of the binary copper complex **2** (Figure 2) shows bands at 705 and 560 nm, which are assigned to the $^2B_{1g} \rightarrow {}^2A_{1g}$ and $^2B_{1g} \rightarrow {}^2E_g$ transitions, respectively, while the absorption band pointed at 370 nm is assignable to charge transfer transition.[30] The spectrum of copper complex **3** (Figure 2) shows a band at 420 nm assignable to the charge transfer.[31]

The X-band ESR spectra of the polycrystalline samples of the copper complexes are recorded at room temperature (298 K). The ESR spectra of these complexes are of axial shape with $g_{11} > g_{\perp} > 2.0023$, characteristic for complexes with $^2\beta_1(d_{x^2-y^2})$ ground state in agreement with the square planar environment of the copper. Both complexes exhibit $g_{11} < 2.3$, suggesting covalent character of the copper ligand bonding in these complexes. The axial symmetry parameter $G = (g_{11}-2)/(g_{\perp}-2)$, which measures the exchange interaction between copper centers in the polycrystalline solid sample of the complex, have also been calculated. According to Hathaway and Billing,[32] if the value of G is above 4, then the exchange interaction is negligible; if, however, the value of G is less than 4, it indicates considerable exchange interaction in the solid complexes. In the complexes reported here, the G value is greater than 4, indicating that interaction is negligible.

Also, the electronic spectra of the iron complex **4** shows charge transfer at 360 nm between the ligand and the metal. In general, the electronic spectra of Fe(III) complexes consist of forbidden transitions, and hence weak bands are often marked charge transfer bands.[33–35] The magnetic moment of this iron (III) complex is 5.82 BM, and it is expected

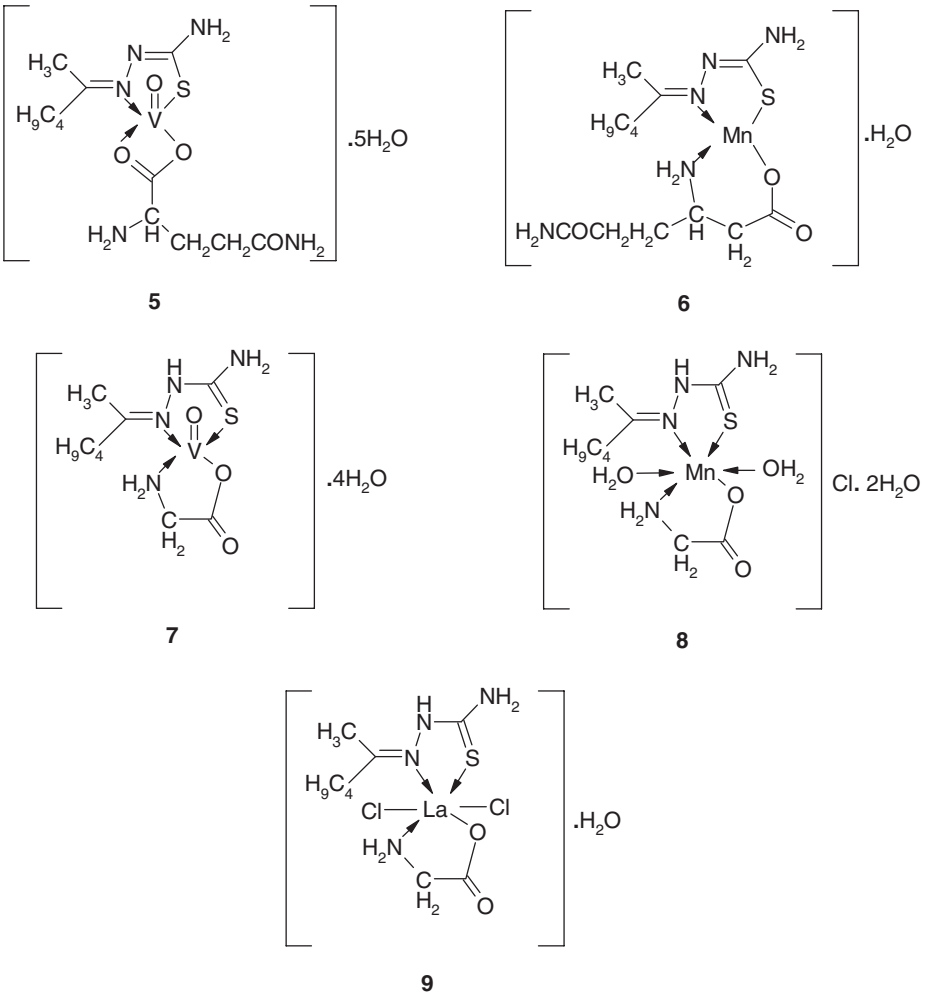


Figure 3 Structure of ternary complexes **5–9**.

that the Fe(III) complex is a high-spin octahedral arrangement ($t_2g^3eg^2$), where the literature magnetic moment values is around 5.92 BM.

Structures of the Ternary Complexes

The electronic spectra of vanadium complexes **5** and **7** (Figure 3) show broad bands at 860 and 840 nm, for the two complexes, respectively, which may be assigned to $^2B_2 \rightarrow {}^2E$ transition, while the other band due to $^2B_2 \rightarrow {}^2B_1$ transition disappeared due to the broadness of the first band.[36] Also, the magnetic moments of these complexes are 1.58 and 1.62 BM, respectively, which confirms that vanadium ions are in the V(IV) state with square-pyramidal geometry.[37] However, the electronic spectra of Mn complexes **6** and **8** show broad bands at 430 and 360 nm, respectively, with their tail to the UV region. These bands, attributable to the spin forbidden d–d transition, are responsible for the color of the

compound.[38] The magnetic moments of the two Mn(II) complexes are 5.85 and 5.90 nm, respectively, corresponding to high-spin configuration due to five unpaired electrons[39] in ground state ^6S ($^6A_1$), in which orbital contribution to the magnetic moment is quenched. The diamagnetic of lanthanum complex **9** has octahedral geometry.

Molar Conductance Data

The metal complexes discussed in this article were dissolved in DMF, and the molar conductivities of 10^{-3} M of their solutions at room temperature were measured to establish the charge of the metal complexes. The conductance data (Table S2) indicate that all binary and ternary complexes, except complexes **2**, **3**, and **8**, have conductivity values in the range characteristic for the non-electrolytic nature, suggesting that these complexes are neutral,[40] whereas copper and manganese complexes have molar conductance of 69.10, 87.42, and 52.9 Ω^{-1} cm^2 mol^{-1}, respectively, which indicates that the chloride ion and acetate groups are uncoordinated.

The molar conductance of complex **2** in DMF is 69.1 Ω^{-1}cm^2 mol^{-1}. Abnormally low conductance value is usually attributed to ion-pair formation resulting from coulombic interactions or to the formation of an intra- or intermolecular hydrogen bond between the counter ion and the imino groups.[41,42]

Biological Activity

As shown in Table S3 (Supplemental Materials), compounds HL (free ligand) and complexes **1**, **5**, **6**, **7**, and **9** inhibited in dose-dependent manner Ehrlich ascites carcinoma (EAC) cells, being observed only for the maximum dose of 25 μg/mL.

The results showed that all six compounds studied have anticancer activity, and the GI_{50} values for these compounds were 21.25, 20.5, 26.25, 17.5, 17.5, and 18 μM, respectively, where the free ligand has minimum antitumor activity that increases in case of the binary complex **1** at 25 μg/mL concentration. This may be attributed to the lipophilic character of the central metal atom explained by Tweedy's chelation theory.[43]

Also, the ternary complexes **5**, **6**, **7**, and **9** showed greater antitumor activity than the free ligand and the binary complex **1** at all concentrations when free amino acids (Glu and Gly) were introduced as secondary ligands.

It should be noted that mixed ligand complexes have a key role in biological chemistry[44] because the mixed chelation occurs commonly in biological fluids, as millions of potential ligands are likely to compete for metal ions in vivo.[40] These create specific structures[44–46] and have been implicated in the storage and transport of active substances through membranes. On the other hand, the complex **5** has more antitumor activity than complex **7**, while the complex **6** showed greater antitumor activity than complex **9** at all concentrations except at 20 μg/mL. This may be explained on the basis that the antiproliferative activity on tumor cells increases with the increase of the alkyl chain greater than 3 carbon atoms. Moreover, it was found that antiproliferative activity of the amide group in Glu is greater than the antiproliferative activity of COOH in free Gly acid.[47]

We can conclude that the two ternary vanadyl complexes **5** and **7** have maximum antitumor activity, which may be due to the fact that vanadyl (IV) is capable of undergoing spontaneous oxidation to vanadate (V) in vivo.[48] Also, studies on antitumor activities of

vanadium compounds have been reviewed extensively.[49] Vanadium compounds seem to exert their antitumor effects mainly through inhibition of cellular protein tyrosine phosphates (PTPs) and/or activation of protein tyrosine kinases (PTKs). Both effects activate signal transduction pathways, leading either to apoptosis and/or to activation of tumor suppressor genes.

CONCLUSION

Metal complexes were prepared by the reaction of HL and metal salts in 1:1, 1:2, or 1:1:1 molar ratios, and their structures were proposed from analytical and spectral data. The biological results suggest that the tested compounds could be used as an alternative to synthetic chemotherapeutic agents. The anticancer activity is in the decreasing order: ternary complexes > binary complexes > the ligand.

EXPERIMENTAL

Materials

All the chemicals used were of A.R. grade. They include 4-methyl-2-pentanone [$(CH_3)_2CH.CH_2COCH_3$], glycine H_2NCH_2COOH, vanadyl sulfate $VOSO_4 \cdot H_2O$, ferric chloride $FeCl_3.6H_2O$ (BDH), manganese chloride $MnCl_2.2H_2O$ (Prolabo), thiosemicarbazide $NH_2CSNHNH_2$, lanthanum chloride $LaCl_3.7H_2O$, copper acetate (Aldrich), nickel chloride $NiCl_2.6H_2O$, copper chloride $CuCl_2.2H_2O$ (Merck), and glutamine $HOOC{-}CH(NH_2){-}CH_2{-}CH_2CONH_2$ (LOBA chemi). The organic solvents used, including absolute ethyl alcohol, methyl alcohol, diethyl ether, and dimethyl sulfoxide (DMSO), were purchased from Merck or Sigma.

Measurements

All the analytical and spectral data were carried out at Central Services Laboratory in the National Research Center, Dokki, Giza, Egypt. The electronic spectra of the ligands and their complexes were carried out using T80+UV/VI spectrometer PG instruments LTD 190–1000. The IR spectra of the ligands and their complexes were measured using a Nexus 670. The ^1H NMR spectra were recorded in chloroform using a JNM-EX270 FT NMR system. The mass spectra were measured with a Jeol JMS-AX500. Molar conductivities in DMF at 25°C were recorded using a model CM-1K-TOA company (Japan) conductivity meter. Magnetic moments at 25°C were determined using the Gouy method with $Hg[Co(SCN)_4]$ as calibrant. Antitumor activity was performed in the National Cancer Institute of Cairo University. The solid ESR spectra of the complexes were recorded with an ELEXSYS E5OO Bruker spectrometer in 3-mm Pyrex tubes at 298 K. Diphenylpicryl hydrazine (DPPH) was used as a g-marker for the calibration of the spectra.

Synthesis of the Ligand

A warm solution of 4-methyl-2-pentanone thiosemicarbazone (MPTSC) (10 g, 0.1 mol) in ethyl alcohol (10 mL) was added to a warm solution of thiosemicarbazide (9.1 g, 0.1 mol) in ethyl alcohol (50 mL), and then 5 drops of concentrated H_2SO_4 acid were added. The mixture was then refluxed at 50°C for about 20 h, and was evaporated to

concentrate the solution where a white precipitate was formed. The precipitate was filtered, washed with ethyl alcohol, then with diethyl ether, and dried under vacuum over anhydrous $CaCl_2$.

^{1}H NMR: δ 8.56 ppm (N_2H), δ 6.45 ppm (N^3H_2), δ 0.86 ppm (CN^1-CH_3) and δ 4.78, 2.11, 0.92 ppm (CH, CH_2, $2CH_3$; C-C_4H_9).

Syntheses of the Metal Complexes

The metal complexes of the ligand HL were prepared by mixing a hot ethanolic solution of the $NiCl_2.6H_2O$, $CuCl_2.2H_2O$, $Cu(Ac)_2$, $FeCl_2.6H_2O$, $VOSO_4{\cdot}H_2O$, $MnCl_2.2H_2O$, and $LaCl_3.7H_2O$ with the required amount of a hot ethanolic solution of the ligand to form 1:1 or 1:2 M/L (metal/ligand) complexes, or in the presence of glycine (Gly) or glutamine (Glu) as a secondary ligand, as shown in Table I. The reaction mixture was then refluxed for a time depending on the transition metal salt used. Some complexes (**5**, **6**, **7**, **8**, and **9**) did not separate upon standing, but only when an aqueous NaOH solution was added under stirring at 40–50°C. The precipitates formed were filtered, washed with ethanol, then with diethyl ether, and dried in a vacuum desiccator over anhydrous $CaCl_2$.

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