Synthesis and spectroscopic characterization of bioactive compounds derived from glutamic acid; study of their antimicrobial and antiproliferative properties

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Abstract: This work was focused on the preparation of glutamic acid derivatives. These compounds were characterize using analytical techniques such as elemental analysis (C, H, N and M), spectral techniques as IR, mass spectra, ^{1}H-NMR, ^{13}C-NMR. The preparation of Metal compounds were carried out by reaction of gluytamic acid derivatives with metal salts such as: **Cu(II), Co(II), Cd(II), Ni(II),Mn(II), and Zn(II)** salts**.** The characterization of the prepared solid compounds using analytical techniques, spectral techniques as UV-VIS, ESR and thermal techniques as TGA and DTA. Also Antimicrobial and antiproliferative. Properties were studied. Some of the prepared compounds show enhanced activity compard with standard drugs.

Keywords: glutamic acid derivatives, metal complexes, analytical, spectral techniques, medical applications.

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INTRODUCTION

1. DEFINITION OF GLUTAMIC ACID

L-Glutamic acid a nonessential amino acid, occurring in proteins, that acts as a neurotransmitter and plays a part in nitrogen metabolism.

L-Glutamic acid plays an important role in the biosynthesis of purine and pyrimidine bases of DNA and RNA [1]. Glutamic acid or glutamate is one of the 20 most common natural amino acids. Glutamic acid is critical for proper cell function, but it is not considered an essential nutrient in humans because the body can manufacture it from simpler compounds [2-3]. In addition to being one of the building blocks in protein synthesis, it is the most widespread neurotransmitter in brain function, as an excitatory neurotransmitter and as a precursor for the synthesis of GABA in GABAergic neurons. Glutamate activates both ionotropic and metabotropic glutamate receptors [4].

2. APPLICATION OF L-GLUTAMIC ACID DERIVATIVES

Schiff bases derived from the reaction of aromatic aldehydes and aliphatic or aromatic amines represented in important series of widely studied organic ligands [5]. A variety of applications such as biological [6-10]. clinical, [11-14] analytical, [15-18] industrial, [19] and catalytically [20-23]. Of Schiff bases and their metal compounds have been reported. Aromatic aldehyde Schiff bases have also attracted much attention due to their diverse biological activities, such as antimicrobial, antibacterial, anti-viral, and anticancer activities [24].

Amino acid methyl esters are important intermediates in organic synthesis, which have been used in various areas such as peptide synthesis [25], medicinal chemistry [26-27].

Quinoxaline derivatives have different pharmacological activities such as bactericides and insecticides [28], antibacterial [29-32], antifungal [29, 33], ant tubercular [29, 34-37, 38], analgesic [37, 38], and anti-inflammatory [38, 39]. The importance of quinoxaline derivatives comes from its nitrogen contents (heterocyclic compounds). the quinoxaline skeleton is also used as an intermediate in designing novel quinoxaline derivatives with potential as anticancer, antimicrobial (or antifungal), antithrombotic and anxiolytic agents and other activity [40]. Metal compounds are made up of a metal ion (the acceptor) and one or more ligands containing the donor atoms. A ligand may be attached to a metal ion by more than one donor atom, thus forming a heterocyclic ring called a chelate ring. In such case the ligand may be termed a chelating agent and the resulting complex a metal chelate [41].

Heterocyclic play an important role in the design and discovery of new pharmacologically active compounds. Recently quinoxalines and related heterocyclic were introduced as prospective potential

chemotherapeutic drug candidate possessing manifold biological activities [42]. Schiff bases derived from an amino and carbonyl compound are an important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively [43]. In azomethine derivatives, the C=N linkage is essential for biological activity, several azomethine has been reported to possess remarkable antibacterial, antifungal, anticancer and antimalarial activities [44].

Experimental

1. Materials

The starting chemicals were of analytical grade and used without further purification.

2. Physical and spectroscopic techniques

The characterization of the compounds carried out using various spectroscopic techniques such as :-

i. Elemental analyses

Elemental analyses (C, H, N and Cl) were performed by analytical laboratory of Cairo University, Egypt.

ii. Molar conductivity

The molar conductivity of 10^{-3} M of compounds in dimethyl-sulfoxide (DMSO) was determined using Bibby conductimeter MCI at room temperature. The molar conductivities were calculated according to the following equation:

$\Lambda M = V*K*g/M_w *\Omega$

Where: Λ_M = molar conductivity (ohm^{-1} cm^2 mol^{-1})

V = volume of the solution (100 cm^3)

K = cell constant: 0.92 cm^{-1}

M_w = molecular weight of the complex

g = grams of complex dissolved in 100 cm^3 solution

Ω = resistance measured in ohms

iii. Mass spectra

The mass spectra of the compounds were recorded on JEOL JMS-XA- 500 mass spectrometer.

iv. Thermal analyses

DTA and TGA were carried out on a Shimadzu DT-30 thermal analyzer in nitrogen atmosphere, from room temperature to 600 °C at a heating rate of 10 °C per minute.

v. ^{1}H-NMR spectra

The ^{1}H-NMR spectra were recorded on a JEOL EX -270 MHZ FT-NMR spectrometer in deuterated dimethylsulfoxide (DMSO - d6) as a solvent. The chemical shifts were measured relative to the solvent peaks.

vi. ^{13}C-NMR spectra

The ^{13}C-NMR spectra were recorded on a Bruker 300 MHz spectrometer with chemical shift values reported in δ units (ppm) relative to an internal standard (tetramethylsilane).

Vii. IR spectra

The infrared spectra of solid compounds were recorded on Perkin Elmer's infrared spectrometer 681 using KBr or CsBr discs.

viii. Electronic absoption spectra

The electronic absorption spectra of the compounds were recorded on UNICO SQ-4802 UV/ Vis. double beam spectrophotometer (190- 1100 nm) using 1 cm quartz cell using DMSO as a solvent.

ix. Magnetic susceptibility

The magnetic susceptibilities of the solid compounds in the solid state were measured in a borosilicate tube with a Johnson Matthey [12]. Magnetic susceptibility Balance at room temperature using the following equations:

$X_a = [2.086\ L\ (R- R^o) / (10^9 W)]$

$X_m = X_a * Mw$

$X_n = X_m – D$

$\mu_{eff} = 2.828\ (X_n \times T)^{1/2}$

Where:-

X_a = mass susceptibility

L = sample length in cm

R = tube + sample reading

R^o = empty the reading

W = mass of the sample

X_m = molar susceptibility

Mw = molecular weight

X_n = corrected molar susceptibility

D = diamagnetic corrections

μ_{eff} = effective magnetic moment

T = room temperature in Kelvin

The theoretical effective magnetic moment value calculated using the equation:

$\mu eff = [n(n+2)]^{1/2}$

Where:

μ_{eff} = theoretical effective magnetic moment

n = the number of the unpaired electrons diamagnetic corrections were made- by interpretation of Pascal's constant.

iix. Determination of metal content

Metal content was determined using colorimetric method on HACH DR 5000 spectrophotometer.

iiix. ESR spectra

The solid ESR spectra of the compounds were recorded with ELEXSYS E500 Bruker spectrometer in 3 nm Pyrex Tubes at 25 ^{o}C. Diphenylpicr-hydrazide (DPPH) free radical was used as a g- marker for the calibration of the spectra. The equation used to determine g- values was

$g = (g_{DPPH})\ (H_{DPPH}) / H$

Where: $g_{DPPH} = 2.0036$

H_{DPPH} = magnetic field of DPPH in gauss

H = magnetic field of the sample in gauss

EXPERIMENTAL

3.PREPARATION OF L-GLUTAMIC ACID DERIVATIVES

3.1. PREPARATION OF COMPOUND (1). methyl4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate.

It was prepared by refluxing of L-glutamic acid (2.5 g, 16.99 mmol) in 30 ml methanol and adding few drops of sulfuric acid, for 4hrs. The mixture solution cooled to r.t. and adding equivalent molar ratio from hydrazine hydrate (1.089 g, 16.99 mmol). To intermediate dimethyl 2-aminosulfatepentanedioate hyd-

rate (4.720 g, 16.99 mmol) produced. And refluxed for 6hrs. The solid product filtered off and washed with methanol to give pure powder of glutamic acid derivatives. Methyl 4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate, white powder, (69%) yield. Physical properties of the compound **(1)** are given in **table (1).**

3.2. PREPARATION OF SCHIFF BASE COMPOUNDS (2&3):

3.2.1.(3Z,5E)-methyl 3-(2-oxo-1-((E)-((E)-3-phenylallylidene)amino)-2-(2-((E)-3-phenylallylidene)hydrazinyl)ethyl)-6-phenylhexa-3,5-dienoate.

It was prepared by refluxing molar ratio (1:3) of methyl 4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate (2.037 g, 7 mmol) in 20 ml diethyl ether and cinnamaldehyde (1.556 g, 21 mmol) for 4hrs. The solution was filtered off and cooled to r.t. The solid product filtered and washed with diethyl ether and recrystallized from ethanol to give pure crystals of glutamic acid hydrazinyl Schiff base derivative. Yellow crystals, (85%) yield. Physical properties of the compound **(2)** are given in **table (1).**

3.2.3. (3E)-methyl 3-(2-hydroxybenzylidene)-4-((E)-(2-hydroxybenzylidene)amino)-5-(2-(2-hydroxybenzylidene)hydrazinyl)-5-oxopentanoate.

It was prepared by refluxing molar ratio (1:3) of methyl 4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate (2.037 g, 7mmol) in 20 ml diethyl ether and salicylaldehyde (2.564 g, 21 mmol) for 4hrs. The solution was filtered off and cooled to r.t. The solid product filtered off and washed with diethyl ether and recrystallized with ethanol to give pure crystals of glutamic acid hydrazinyl Schiff base derivative. Yellow crystals, (85%) yield. Physical properties of the compound **(3)** are given in **table (1).**

2.3- synthesis of new Schiff bases azo dyes (4&5):

Synthesis of azo dyes precursors. A general procedure.

To a solution of an aniline derivative (10 mmol) in water (5 mL), concentrated hydrochloric acid (20 mL) was added slowly with stirring. The clear solution was poured into ice water mixture, diazotied with sodium nitrite (0.69 g, 10 mmol), dissolved in water (3.5 mL), during a period of 15 min at 0-5 ^{O}C. The cold diazo solution was added drop wise to the solution of salicyladehyde (1.05 mL, 10 mmol) in water (50 mL) containing sodium hydroxide (0.4 g) and sodium carbonate (7.3 g) during a period of 30 min at 0-5 ^{O}C. The reaction mixture was stirred for 1 hr. in ice bath, allowed to warm slowly to room temperature and subsequently stirred for 4 hr. at this temperature. The product was collected by filtration and recrystallized from mixture of EtOH and H_2O.

2.3.4-(3E)-methyl 4-((E)-4-((4-phenyl)diazenyl)-2-hydroxybenzylidene)amino)-5-(2-(4((4- phenyl)diazenyl)-2-hydroxybenzylidene)hydrazinyl)-5- oxo pe ntanoate.

azo dye 2-hydroxy-4-(phenyldiazenyl) benz aldehyde (1.816 g, 8mmol) in EtOH (20 mL) were added to a solution of methyl 4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate (1.164 g, 4mmol) in ethanol (20 mL). The reaction mixture was stirred for 2hr. The products were collected by filtration and recrys-tallized from ethanol, yellowish brown crystals, (77%) yield. Physical properties of the compound are given in **table (1).**

2.3.5- (3E)-methyl 4-((E)-4-((4-chlorophenyl)diazenyl)-2-hydroxybenzylidene)amino)-5-(2-(4((4-chlorophenyl)diazenyl)-2-hydroxybenzylidene)hydrazinyl)-5-oxopentanoate.

Azo dye 4-((4-chlorophenyl)diazenyl)-2-hydroxybenzaldehyde (2.092 g, 8mmol) in EtOH (20 mL) were added to a solution of methyl 4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate (1.164 g, 4 m mol) in ethanol (20 mL). The reaction mixture was stirred for 2hr. The products were collected by filtration and recrystallized from ethanol, yellow crystals, (83%) yield. Physical properties of the compound **(5)** are given in **table (1)**.

2.3- synthesis of quinoxalin:

General procedures

Synthesis of quinoxalin-2, 3-dione

To a mixture of o-Phenylenediamine (27.9g, 0.25 mole) and **oxalic acid** (32.5g, 0.36 mole) 4N HCl (150ml) was added and refluxed in an oil bath for 1 hr and cooled. The crude solid that separated out was filtered off, washed and recrystallized from ethanol. The yield of the product was (86%) yield. mp.> 300 ^{o}C.

Synthesis of 2, 3-dichloroquinoxaline

An equimolar quantity of quinoxalin-2,3-dione (16.01g, 0.10 mole) was treated with phosphorous oxychloride (15.33g, 0.10 mole) at room temperature and allowed to stand for 1 hr. The resultant product obtained was recrystallized from ethanol. The yield of the product was (82%) yield. mp. 264-268 ^{o}C.

2.3.6-methyl 4-(1H-[1, 3,4]oxadiazino[5,6-b]quinoxalin-3-yl)-2-aminosulfatebutanoate.

methyl 4-aminosulfate-5-hydrazinyl-5-oxopentanoate hydrate (2.91 g 0.01 mole) and 2,3-dichloro quinoxaline (1.99 g, 0.01mole) were dissolved in N,N-dimethylformamide (40 ml). The reaction mixture was refluxed for 5 hours, cooled and poured into crushed ice. Periodically, sodium carbonate solution (0.005, 0.53g in 10 ml water) was added to neutralize HCl evolved during the reaction. After completion, the solid separated out was filtered off, washed with water, dried and recrystallized from alcohol. Red crystals, (80%) yield. Physical properties of the compound **(6)** are given in **table (1)**.

2.3- synthesis of quinoxalin glutamic acid derivatives (7):

2.3.7-methyl 4-(1H-[1,3,4]oxadiazino[5,6-b]quinoxalin-3-yl)-2-aminosulfatebutanoate

L-glutamic acid (1.47 g 0.01 mole) and 2,3-dichloro quinoxaline (1.99 g, 0.01 mole) were dissolved in N,N- dimethylformamide (40 ml). The reaction mixture was refluxed for 5 hours, cooled and poured into crushed ice. Periodically, sodium carbonate solution (0.005, 0.53g in 10 ml water) was added to neutralize HCl evolved during the reaction. After completion, the solid separated out was filtered off, washed with water, dried and recrystallized from alcohol. White transparent, (60%) yield. Physical properties of the compound **(7)** are given in **table (1)**.

2.3.8. 2-((2-hydroxybenzylidene)amino)-N1,N5-bis (2-((Z)-(2-hydroxybenzylidene) amino)ethyl) pentanediamide.

It was prepared by refluxing of L-glutamic acid (2.5 g,16.99 mmol) in 30 ml methanol and adding few drops of sulfuric acid, for 4hrs. The mixture solution cooled to r.t. Adding molar ratio(2:1) from ethylene diamine (2.045 g, 33.98 mmol). To intermediate dimethyl 2-aminosulfatepentanedioate hydrate (5.012 g, 16.99mmol) produced. and refluxed for 6hrs. The solid product filtered off and washed with methanol to give pure powder of glutamic acid derivative, 2-amino-N^1,N^5-bis(2-aminoethyl)pentanediamide.

Refluxing molar ratio (1:3) of 2-amino-N^1,N^5-bis(2-aminoethyl)pentanediamide (1.617 g, 7 mmol) in 20 ml diethyl ether and salicylaldehyde (2.564 g, 21 mmol) for 4hrs. The solution was filtered off and cooled to r.t. The solid product filtered off and washed with diethyl ether and recrystallized from ethanol to give pure crystals of 2-((2-hydroxybenzylidene)amino)-N^1,N^5-bis(2-((Z)-(2-hydroxy benzylidene)amino)ethyl)pentanediamide. Yellow crystals, (80%) yield. Physical properties of the compound **(8)** are given in **table (1)**.

2.3.9. (1Z,5E)-2-((2-hydroxybenzylidene)amino)-N1,N5-bis(2-((Z)-(2-hydroxybenzylidene)amino)ethyl) pentanebis(hydrazonamide)

It was prepared by stirring molar ratio (1:2) 2-((2-hydroxybenzylidene) amino)-N1,N5-bis(2-((Z)-(2-hydroxybenzylidene)amino)ethyl)pentanediamide. (2.715 g, 5mmol) with hydrazine hydrate (1.280 g, 10 mmol) for 2hr. The solid product filtered off and washed with ethanol and recrystallized from ethanol. Off white powder, (78%) yield. Physical properties of the compound **(9)** are given in **table 1**.

2.3.10-2-aminosulfate-N1,N5-bis(2-aminophenyl) pentanediamide.

It was prepared by refluxing molar ratios (1:2) from dimethyl 2-aminosulfatepentanedioate hydrate (2.36 g, 8 mmol) with benzene-1,2-diamine (1.7296 g, 16 mmol) in 20 ml ethanol, for 1hr. The solid product filtered off and washed with ethanol and recrystallized from ethanol. Off white powder, (60%) yield. Physical properties of the compound **(10)** are given in **table (1)**.

2.3.11-2-aminosulfate-N1-(2-((E)-(2-hydroxybenzylidene)amino)phenyl)-N5-(2-((Z)-(2-hydroxybenzylidene)amino)phenyl)pentanediamide.

it was prepared by refluxing molar ratios (1:2) from 2-aminosulfate-N^1,N^5-bis(2-aminophenyl) pentanediamide. (2.575 g, 5 mmol) with 2-hydroxybenzaldehyde (1.22 g, 10 mmol) in 20 ml ethanol, for 1hr. The solid product filtered off and washed with ethanol and recrystallized from ethanol. Light gray powder, (75%) yield. Physical properties of the compound **(11)** are given in **table (1)**.

2.3.12-2-aminosulfate-1,5-bis(quinoxalino[2,3-b]quinoxalin-5(12H)-yl)pentane-1,5-dione

2-aminosulfate-N^1,N^5-bis(2-aminophenyl)-pentanedia- mide (2.57 g 0.05 mole) and 2,3-dichloro quinoxaline (0.995 g, 0.05 mole) were dissolved in N,N-dimethylformamide (40 ml). The reaction mixture was refluxed for 5 hours, cooled and poured into crushed ice. Periodically, sodium carbonate solution (0.005, 0.53g in 10 ml water) was added to neutralize HCl evolved during the reaction. After completion, the solid separated out was filtered off, washed with water, dried and recrystallized from alcohol. Red crystals, (80%) yield. Physical properties of the compound **(12)** are given in **table (1**).

3.2 PREPARATION OF METAL COMPOUNDS OF GLUTAMIC ACID DERIVATIVES

Compounds (13&17): Alcoholic solution of 0.004 mol of $MSO_4.nH_2O$, where M= Cu(II) and Ni(II) was added to an alcoholic solution of 0.004 mol of the compound **(1).** The mixture was stirred at room temperature for 40 min and warmed on water bath for 4 hr. On standing overnight, the precipitated product was obtained which was filtered off, washed with water, then with ethanol and recrystallized from hot alcoholic solution. The product was then washed with ethanol, ether and dried in vacuum for 3 hr.

Compounds (14&15): Alcoholic solution of 0.002 mol of $M(CH_3COO)_2.nH_2O$, where M=Co(II) and Mn(II) was added to an alcoholic solution of 0.004 mol of the compound **(1).** using the above procedure.

Compounds (16&18): Alcoholic solution of 0.004 mol of $M(CH_3COO)_2.nH_2O$, where M=Zn(II) and Cd(II) was added to an alcoholic solution of 0.004 mol of the ligand (1). using the above procedure.

Compound (19): Alcoholic solution of 0.002 mol of $Cu(CH_3COO)_2.4H_2O$ was added to an alcoholic solution of 0.004 mol of the compound **(4).** using the above procedure.

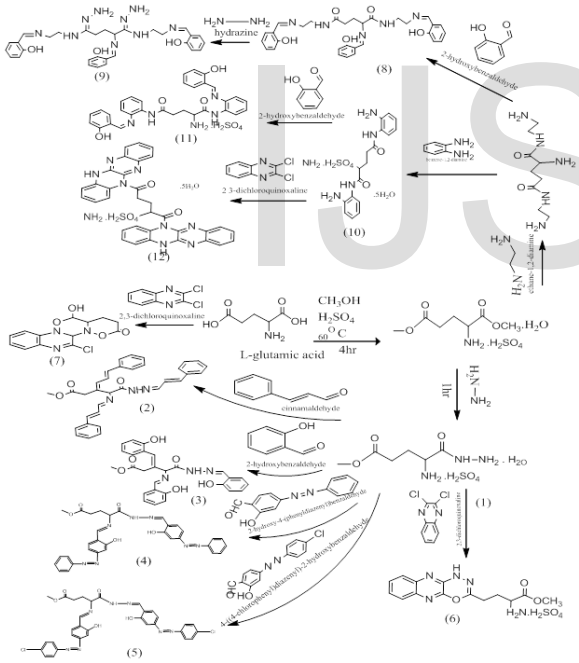
Compound (20): Alcoholic solution of 0.002 mol of $Cu(CH_3COO)_2.4H_2O$ was added to an alcoholic solution of 0.004 mol of the compound **(5).** using the above procedure.

Compound (21): Alcoholic solution of 0.002 mol of $Zn(CH_3COO)_2.4H_2O$ was added to an alcoholic solution of 0.004 mol of the compound (6). using the above procedure.

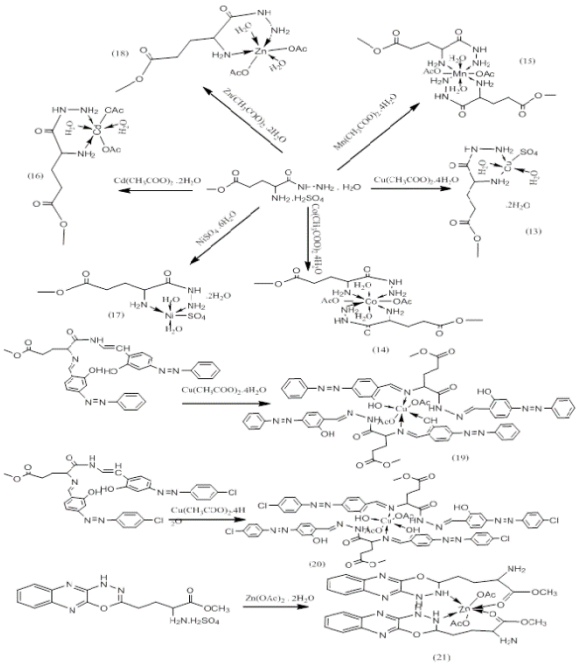
RESULTS AND DISCUSSION

I. PREPARATION AND INVESTIGATION OF L-GLUTAMIC ACID DERIVATIVE AND ITS COMPLEXES:

The elemental analyses, spectral data (Tables 1-5) and thermal analyses (Table 6) reveal that, the compounds formed are colored, stable in air; soluble in polar solvents such as DMF and DMSO and ethanol, $CHCl_3$ and benzene. All the compounds are non-electrolytes. Many attempts were made to grow diffract able crystal, but unfortunately no crystal has been obtained until now. The preparation of compounds **(1), (2), (3), (4), (5), (6), (7), (8), (9), (10), (11) and (12).** are shown in ***scheme 1***. The reaction of compoud **(1)** with metal ions in ethanol led to the formation of compounds **(13)-(18).** The reaction of compound **(4)** with metal ions in ethanol led to the formation of compound **(19).** The reaction of compound **(5)** with metal ions in ethanol led to the formation of compound **(20).** The reaction of compound **(6)** with metal ions in ethanol led to the formation of compound **(21).** The preparation of compounds **(13), (14), (15), (16), (17), (18), (19), (20) and (21).** are shown **in *scheme 2*.**



Scheme (1). Preparation of compounds (1), (2), (3), (4), (5), (6), (7), (8), (9), (10), (11) and (12).



Scheme (2). Preparation of compounds (13), (14), (15), (16), (17), (18), (19), (20) and (21).

Table(1):-Analytical and Physical Data of the prepared compounds.

No.	Ligands/Complexes	Color	FW	M.P (°C)	Yield (%)	Anal. /Found (Calc.) (%)			
						C	H	N	M
(1)	$C_9H_{17}N_3O_4S$	white	291	190	69	24.74 (24.6)	5.88 (5.7)	14.4 (14.2)	
(2)	$C_{15}H_{13}N_3O_2$	yellow	517.2	>260	85	76.57 (76.4)	6.04 (5.9)	8.12 (8)	
(3)	$C_{25}H_{23}N_5O_4$	yellow	487.5	>260	85	66.5 (66.34)	5.13 (4.95)	8.6 8.45	
(4)	$C_{25}H_{21}N_5O_5$	yellowish brown	591	>260	77	64.97 (64.7)	5.2 (5)	16.5 (16.4)	
(5)	$C_{32}H_{23}N_7O_5Cl_2$	yellow	662	>260	83	58 (57.7)	4.3 (4.14)	14.8 (14.7)	
(6)	$C_{16}H_{12}N_2O_5S$	Red	399	>260	80	42.1 (42)	4.2 (4.1)	17.5 (17.38)	
(7)	$C_{12}H_{12}N_2O_4$	White transparent	309.5	>260	60	50.4 (50.1)	3.8 (3.65)	13.5 (13.4)	
(8)	$C_{29}H_{23}N_5O_5$	yellow	543.2	>260	80	66.2 (66.15)	6.12 (6)	12.88 (12.7)	
(9)	$C_{30}H_{21}N_9O_3$	Off white	571.6	>260	78	63.03 (62.9)	6.52 (6.4)	22.05 (21.93)	
(10)	$C_{17}H_{20}N_4O_{11}S$	Off white	515	>260	60	39.6 (39.56)	6.4 (6.31)	13.59 (13.5)	
(11)	$C_{21}H_{21}N_3O_4S$	Light gray	633	>260	75	58.76 (58.7)	4.93 (4.86)	11.05 (11)	

Continued Table (1):-

(12)	$C_{22}H_{22}N_8O_{11}S$	yellow	767	>260	55	51.6 (51.66)	4.8 (4.75)	16.4 (16.35)	
(13)	$C_8H_{21}N_2O_{11}SCu$	Faint blue	406.54	>260	88	17.71 (17.47)	5.16 (4.95)	10.33 (10.14)	15.62 (15.32)
(14)	$C_{16}H_{32}N_4O_{12}Co$	violet	562.9	>260	80	34.1 (34.06)	6.4 (6.4)	14.9 (14.85)	10.46 (10.3)
(15)	$C_{14}H_{38}N_4O_{12}Mn$	Light brown	558.9	>260	85	34.35 (34.3)	6.4 (6.32)	15 (14.97)	9.8 (9.77)
(16)	$C_{10}H_{22}N_2O_9Cd$	Light violet	441.41	>260	76	27.18 (27.09)	5.2 (5.13)	9.5 (9.35)	25.46 (25.4)
(17)	$C_8H_{22}N_2O_{11}SNi$	Faint green	401.69	>260	79	17.92 (17.6)	5.22 (5.16)	10.45 (10.35)	14.6 (14.48)
(18)	$C_{10}H_{22}N_2O_9Zn$	White	394.38	>260	83	30.42 (30.3)	5.82 (5.72)	10.64 (10.57)	16.57 (16.38)
(19)	$C_{88}H_{80}N_{14}O_{14}Cu$	Brown	1363.53	>260	85	59.8 (59.73)	4.69 (4.62)	14.37 (14.22)	4.65 (4.6)
(20)	$C_{88}H_{82}N_{14}O_{14}CuCl_4$	Brown	1501.54	>260	85	54.34 (54.16)	3.99 (3.81)	13.05 (13)	4.23 (4.2)
(21)	$C_{42}H_{36}N_{10}O_{12}Zn$	Red	787.38	>260	88	48.76 (48.55)	4.82 (4.63)	17.78 (17.76)	8.3 (8.29)

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Table (2):- IR Frequencies of the Bands (cm^{-1}) of the prepared compounds.

No.	ν(H2O /OH)	ν(N-H)	ν(C-O)/ (C-OH)	ν(C=O)	ν(C=N)	ν(C=C) Ar / al	ν(H-bond.)	ν(OAc)/ SO4/Cl	ν(M-O)	ν(M-N)
(1)	3600	3500-3431 3300	-	1732-1660	-	-	3650-3310 3067-2680	1112-1014 618	-	-
(2)	-	3435	-	1750-1627	1586-1447	1440-871	3854-3024		-	-
(3)	3434	3050	1271-1200 1151-1032	1796-1619	1571-1478	1450-890	3038-2921 2849-2747		-	
(4)	3436	3050	1271-1189 1102-998	1797-1622	1571	1425-855	2922	-		-
(5)	3436	3048	1272-1194 1151-1009	1623-1593	1523	1479-890	3751-2925	460	-	-
(6)	-	3428-3102	-	1843-1730	1452	889-877	3858-3038 2930	647	-	-
(7)	3432	3100	1267-1178 1114-990	1631	1460-1455	877-865	3590-3038 2980	595	-	-
(8)	3426	3250	1283-1205 1148-1097	1631-1577	1494-1456	1415-856	3751-3600 3049-2901	-	-	-
(9)	3442	3381-3286	1267-1197 1149-1095	-	1574148 8	1402-893	3817-3943 3038-2926	-	-	-

Continued Table (2):-

(10)	3600	3448-3352 3239	-	1635-1571	-	880-850	3500-2914	849	-	-
(11)	3445	3320-3224	1307-1249 1035-1051	1623-1560	1502	1460-879	3048-2926 2863-2737	851	-	-
(12)	3550-3390	3100-3438	-	1642-1630	1640	875-860	3837-3741 2938-3038	882	-	-
(13)	3423	3264-3226 3129	-	1626-1615	-	-	3912-2952 2677	1084-677	617	558
(14)	3600-3550	3427-3268	-	1729-1619	-	-	3150-3070 2955	1418-1390	611	485
(15)	3600-3550	3361-3200	-	1671-1540	-	-	3008-2700	1418-1296	616	555
(16)	3550-3500	3425-3278 3147	-	1636-1573	-	-	3838-3075 2923-2653	1508-1428	617	577
(17)	3650-3600	3422-3291 3238-3162	-	1735-1628	-	-	3904-3064 2956	1109-808	618	539
(18)	3650-3400	3281-3166	-	1629-1573	-	-	3075-2947 2670	1508-1323	614	480
(19)	3432	3200-3100	1322-1254 1153-1112	1607	1529	1464-834	3800-2918	1374-1322	596	529
(20)	3425	3200-3150	1318-1274 1198-1150	1608-1590	1506	1441-895	3750-2924	1318-1274	593	512
(21)	-	3439-3103	-	1690-1639	1479	1450-881	3600-3040 2936	1343-1267	597	523

Table (3,a):-Mass spectrum of the compound (1).

m/z	Rel. Int.	Assignments
55	32	C_4H_7
71	21	C_4H_7O
84	100	C_5H_8O
100	6	$C_5H_8O_2$
116	41	$C_5H_8O_3$
185	13	$C_5H_{15}O_6N$
199	7	$C_5H_{15}O_6N_2$
213	9	$C_5H_{15}O_6N_3$
229	8	$C_5H_{15}O_7N_3$
242	14	$C_6H_{16}O_7N_3$
259	5	$C_6H_{17}O_8N_3$
291	25	$C_6H_{17}O_8N_3S$

Table (3,b):- Mass spectrum of compound(13).

m/z	Rel. Int.	Assignments
55	71	C_3H_3O
57	100	C_3H_5O
71	67	C_3H_5NO
85	14	$C_3H_5N_2O$
181	5	$C_3H_5N_2O_7$
198	5	$C_3H_6N_2O_8$
217	6	$C_3H_9N_2O_9$
233	5	$C_3H_9N_2O_{10}$
263	7	$C_4H_{11}N_2O_{11}$
293	6	$C_5H_{15}N_3O_{11}$
305	7	$C_6H_{15}N_3O_{11}$
337	6	$C_6H_{15}N_3O_{11}S$
406	22	$C_6H_{15}N_3O_{11}SCu$

A. MASS SPECTRA:

The mass spectrum of the compound **(1),** Table (3,a) revealed a molecular ion peak (m/z) at 291 a.m.u which is coincident with the formula weight of the ligand and supports the identity of the Structure. Furthermore, the fragments observed at m/z = 55, 71, 84, 100, 116, 185, 199, 213, 229, 242, 259 and 291 corresponding to C_4H_7, C_4H_7O, C_5H_8O, $C_5H_8O_2$, $C_5H_8O_3$, $C_5H_{15}NO_6$, $C_5H_{15}N_2O_6$, $C_5H_{15}N_3O_6$, $C_5H_{15}N_3O_6$, $C_5H_{15}N_3O_7$, $C_6H_{16}N_3O_7$, $C_6H_{17}N_3O_8$ and $C_6H_{17}N_3O_8S$ moietiesrespectively. The Cu(II) compound (13), (chart 8), Table (3,b) spectrum show a peak (m/z) at 406 a.m.u corresponding to the formula weight of the compound. Additionally, the peaks observed at 55, 57, 71, 85, 181, 198, 217, 233, 263, 293, 305, 337 and 406 are due to C_3H_3O, C_3H_5O, C_3H_5NO, $C_3H_5N_2O$, $C_3H_5N_2O_7$, $C_3H_6N_2O_8$, $C_3H_9N_2O_9$, $C_3H_9N_2O_{10}$, $C_4H_{11}N_2O_{11}$, $C_5H_{15}N_3O_{11}$, $C_6H_{15}N_3O_{11}$, $C_6H_{15}N_3O_{11}S$ and $C_6H_{15}N_3O_{11}SCu$ moieties respectively .

B. CONDUCTIVITY

The molar conductivity of 1×10^{-3} M solution of the compounds (13-21) in DMSO at room temperature are given in experimental section. The value of molar conductance of all compounds are in the 5.9-8.1 $\Omega^{-1}cm^2mol^{-1}$ range, indicating a non-electrolytic nature of these compounds, confirming the involvement of the acetate and sulfate anions in the coordination sphere.

C. INFRARED SPECTRA

Important spectral bands of the compounds are presented in Table (2). The IR spectrum of the **compounds (1), (2), (3), (4), (5), (6), (7), (8), (9), (10), (11) and (12)**. showed broad medium intensity bands in the 3600–3310 and 3067-2650 cm^{-1} ranges, which are attributed to intra- and intermolecular hydrogen bondings. The broad medium bands at 3500 and 3048cm^{-1} are assigned to the υ(NH) groups. compoundds **(1), (2), (3), (4), (5), (6), (7), (8), (10), (11) and (12)** bands observed around 1843-1560 cm^1ranges, characteristic to the carbonyl υ(C=O) groups. The compounds **(3), (4), (5), (9) and (11)** showed broad medium bands at 3432-3445cm^{-1} ranges, are assigned to the υ(OH) group. Compounds **(2), (3), (4), (5), (6), (7), (8), (9), (11) and (12)** bands observed around 1640-1447 cm^1ranges, characteristic to the carbonyl υ(C=N) groups. IR spectrum of the compounds **(3), (4), (5), (7),**

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(8), (9) and (11) showed bands around 1307-1178 and 1151-990 cm^{-1} ranges, characteristic to υ(C-O)/υ(C-OH) groups. The IR spectrum of the **compounds (2), (3), (4), (5), (6), (7), (8), (9), (10), (11) and (12)** showed bands in the 1450–1402 and 893-855 cm^{-1} ranges, characteristic to υ(C=C)Ar/Al. IR spectrum of the compounds **(1), (6), (10), (11) and (12)** showed bands around 1112 and 618 cm^{-1}ranges, characteristic to υ(SO_4) group. IR spectrum of the compounds **(5)** and **(7)** showed bands around 596 and 460 cm^{-1}ranges, characteristic to υ(Cl) group. IR spectrum of the compounds **(1), (10) and (12)** showed bands around 3600 and 3500 cm^{-1} ranges, characteristic to H_2O.

Table (2) indicate Neutral bidentate ligand: coordinating through di NH_2 group as in compounds **(13), (16), (17) and (18).**This mode of coordination is supported by the following evidences:(i) the amine groups (NH_2) stretching vibrations were shifted to lower wave numbers, suggesting coordination of the amine nitrogen atoms to the metal ion. (ii) The appearance of new bands in the 577-480cm^{-1} regions are corresponding to the υ(M-N) vibrations respectively. Table (2) indicate Neutral tetra dentate ligand: coordinating through tetra NH_2 group as in compounds **(14) and (15).** This mode of coordination is supported by the following evidences:(i) the amine groups (NH_2) stretching vibrations were shifted to lower wave numbers, suggesting coordination of the amine nitrogen atoms to the metal ion. (ii) The appearance of new bands in the 577-480cm^{-1} regions are corresponding to the υ(M-N) vibrations respectively.

Neutral tetradentate ligand: coordinating through the two OH and the two NH_2 groups as in compounds **(19) and (20).** Coordinating through two OH, two amine groups This mode of coordination is supported by (i) vibration band of the C=N was shifted to lower wave number with a decreasing its intensity while the other one band appeared in its original place. (ii) the appearance of the band for the hydroxyl OH, Table (2) indicating at low value the coordination to the metal ion . (iii) The appearance of new bands in the 512 and 593 cm^{-1} regions are due to the υ(M-N) and υ(M-O) vibrations respectively. Neutral tetradentate ligand: coordinating through two C=O and two NH_2 group as in compound **(21).**This mode of coordination is supported by the following evidences:(i) the amine groups (NH_2) stretching vibrations were shifted to lower wave numbers, suggesting coordination of the amine nitrogen atoms to the metal ion. (ii) The appearance of new bands in the 523cm^{-1} regions are corresponding to the υ(M-N) vibrations respectively. bands observed around 1690 and 1639 cm^1, characteristic to the carbonyl (C=O) stretching vibrations were shifted to lower wave numbers, suggesting coordination of the carbonyl oxygen atoms to the metal ion. (iii) The appearance of new bands in the 597 cm^{-1} regions which are assigned to υ(M-O) vibrations respectively. The presence of water molecules within the coordination sphere in all compounds were supported by the presence of weak bands around 3600-3423 cm^{-1} due to OH stretching, H_2O deformation, H_2O rocking and H_2O wagging, respectively. The appearance of two characteristic bands in the 1418-1390 , 1418-1296, 1508-1428, 1508-1323, 1374-1322, 1318-1274 and 1343-1267 cm^{-1} ranges in the spectra of compounds **(14), (15), (16), (18), (19), (20) and (21)** were attributed to $\upsilon_{asym.}(COO^-)$ and $\upsilon_{sym.}(COO^-)$ respectively, indicating the participation of the acetate oxygen in the compound formation. Compounds spectra demonstrated strong to medium bands at 1109-1084 and 808- 677 cm^{-1} belonging to the antisymmetric and symmetric stretching modes of the sulfate group. These values are consistent with that reported for the sulfate species coordinating to the M(II) in an bidentate fashion for compounds **(13) and (17).**

D. ELECTRONIC SPECTRA AND MAGNETIC MOMENT

DMF electronic absorption spectral bands as well as room temperature effective magnetic moment values of the compounds are reported in **(Table 4).**

Copper (II) compounds (13) and (19)-:

The electronic spectral data of copper (II) compounds **(13) and (19)** are shown in (Table 4). The compounds showed bands in the 230-298, 337-390, 450-480, 610-615 and 733-734 nm ranges. The first two bands are assigned to π→π* and n→π* transitions within the ligand and the other bands are due to $^2B_{1B} \rightarrow {}^2A_{1g} \rightarrow {}^2B_{1g} \rightarrow {}^2E_g$ and $^2B_{1g} \rightarrow {}^2B_{2g}$ transitions respectively, indicating that, the copper(II) compounds have distorted octahedral geometry**.** The magnetic moments for copper(II) compounds **(13) and (19)** at room temperature are in the 1.67-1.7 B.M. range, indicating that, the compounds have octahedral or square planar geometry. The apparent lower values of complexes may be assigned to spin-spin interactions take between copper (II) ions through molecular interactions.

Cobalt (II) compound (14)-:

The electronic spectra of the Co(II) compound **(14)** exhibit three transition bands at 420,550 and 734 nm. These bands are assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)(\nu_1)$, transitions respectively, corresponding to high spin cobalt(II) octahedral compounds. The magnetic moments of compound **(14)** is 4.98, which are well within the reported range of high spin octahedral Co(II) compounds.

Manganese(II) compound (15)-:

Absorption spectra of manganese (II) compound **(15)** showed bands at 570, 620 nm. These two bands can be assigned to$^5B_{1g} \rightarrow {}^5E_g$ and $^6B_{1g} \rightarrow {}^6A_{2g}$ transitions respectively, suggesting an distorted octahedral arrangement around the manganese(II) ion. The magnetic moments of compound **(15)** is 6.8, which are well within the reported range of high spin octahedral manganese (II) compound.

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Nickle (II) compound (17)-:

The electronic absorption spectra of Ni(II) compound **(15)** displayed three bands at 247, 268 and 380 ranges, these bands are corresponding to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\upsilon_1)$ transitions respectively, indicating octahedral nickel (II) compound. The magnetic moment value of nickel (II) compoud **(15)** 2.93 B.M, which are consistent with two unpaired electrons state and confirming octahedral geometry around nickel (II) ions.

Zinc (II) compounds (18) and (21)-:

The electronic spectral data of Zinc (II) compounds **(18) and (21)** are shown in (Table 4). The compounds showed bands in the 256-280, 324-390, 440-575and 610-733 nm ranges. The first two bands are assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions within the ligand and the other bands are due to $^2B_{1B} \rightarrow {}^2A_{1g} \rightarrow {}^2B_{1g} \rightarrow {}^2E_g$ and $^2B_{1g} \rightarrow {}^2B_{2g}$ transitions respectively, indicating that, the Zinc(II) compounds have octahedral geometry. The magnetic moment of zinc(II) compounds **(18) and (21)** show diamagnetic values.

Table (4):- Electronic Spectra (nm) and Magnetic Moments (B.M) for the compound (13), (14), (15), (17), (18), (19) and (21).

Comp. No.	λ_{max} (nm)	μ_{eff} (BM)	υ_2/υ_1
(13)	230,257,275,296,380,450,615,734	1.67	-
(14)	275,375,420,550,600,734	4.98	-
(15)	258,270,298,350,410,570,620,725	6.8	-
(17)	247,268,380	2.93	-
(18)	256,280,325,440,575,610,733	Diamagnetic	-
(19)	235,258,337,390,480,615,733	1.7	-
(21)	256,324,338,390	Diamagnetic	-

E. ^{1}H NMR SPECTRA

The ^{1}H NMR spectrum of compound **(2)** exhibits: 2.51 (2H, -CH2); 3.35(3H, -OCH3); 7.092–7.667 (15H, aromatic protons); 8.4(1H, CH=N-proton). The ^{1}H NMR spectrum of compound **(3)** exhibits: (2H, -CH2); 3.35(3H, -OCH3); 6.934–7.7 (12H, aromatic protons); 9.013(1H, CH=N- proton); 11.11(N-H…O=C-)[9]. The ^{1}H NMR spectrum of compound **(6)** exhibits: 2.51(2H, -CH2); 3.31(2H, NH2); 7.931–8.064 (4H, aromatic protons). The ^{1}H NMR spectrum of compound **(7)** exhibits: 2.49(2H, -CH2); 3.31(2H, NH2); 7.927–7.95 (4H, aromatic protons); 8.098(1H, OH). The ^{1}H NMR spectrum of compound **(11)** exhibits: 2.507(2H, -CH2); 5.49(2H, OH); 6.6–7.709 (16H, aromatic protons); 9.9 (N-H…O=C-) [45].

F. ^{13}C- NMR SPECTRA

The ^{13}C-NMR of compound **(6):** δ 144.478, 139.921, 131.646, 127.791, 40.274. The ^{13}C-NMR of compound **(7):** δ 144.630, 140.069, 131.809, 127.943, 120.639, 40.403. The ^{13}C-NMR of compound **(10):** δ 130.318, 121.667, 119.102, 39.940. ^{13}C-NMR of compound **(11):** δ 157.830, 154.673, 150.761, 133.774, 130.200, 123.120, 118.171, 112.015, 62.451, 44.087, 40.308, 25.131.

G. ELECTRON SPIN RESONANCE (ESR)

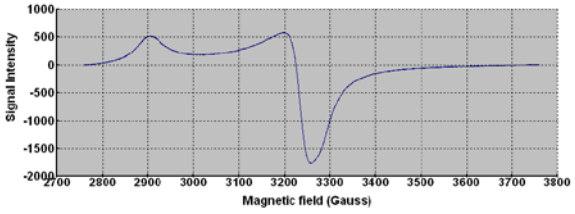
The ESR spectral data for metal compounds (13), (14), (15), (19) and (20) are presented in **Table (5).** The spectra of copper(II) compounds (13), (19) and (20) are characteristic of species, d^9, configuration and having axial type of a $d(x^2\text{-}y^2)$ ground state which is the most common for copper(II) compounds [46,47]. The compounds showed $g_{\parallel} > g_{\perp} > 2.03$, indicating octahedral geometry around the copper(II) ion [48]. The expression G is related to g-values, $G = (g_{\parallel}-2)/(g_{\perp}-2)$. If $G > 4.0$, then local tetragonal axes are misaligned parallel or only slightly misaligned and if $G < 4.0$, significant exchange coupling is present [49]. Compounds showed values indicating spin–exchange interactions takeplace between the copper(II) ions, which is consistent with the magnetic moments values(Table 5). Also, the $g_{\parallel}/A_{\parallel}$ values are considered as a diagnostic of stereochemistry. The $g_{\parallel}/A_{\parallel}$ values lie just within the range expected for the octahedral compounds [50]. The orbital reduction factors ($K_{\parallel}$, $K_{\perp}$, K), which are a measure of covalence were also calculated [48]. K values, for the copper(II) compounds (13) (19) and (20), indicating covalent bond character [51]. Also, the g-values show considerable a covalent bond character.

The in-plane σ- covalency parameter, α^2 (Cu) suggests a covalent bonding. The compounds show β^2values indicating ionic character in the in-plane β_1^2 bonding. While Compounds (14) and (15) show isotropic spectra.The calculated orbital populations (a^2d) for the copper(II) compounds indicate a $d(x^2\text{-}y^2)$ ground state [49,52] .while β_1^2 of compounds show covalent bond caracter in the out of plan.

Table (5): ESR data for the metal compounds.

No.	$g_{\parallel}$	$g_{\perp}$	g_{iso}[a]	$A_{\parallel}$ (G)	$A_{\perp}$ (G)	A_{iso}[b] (G)	G[c]	$\Delta E_{x^2-y^2}$ (cm^{-1})	$\Delta E_{xz,yz}$ (cm^{-1})	$K_{\parallel}^2$	$K_{\perp}^2$	K	$g_{\parallel}/A_{\parallel}$ (cm^{-1})	α^2	β^2	β_1^2	-2B	a^2d^9
(13)	2.19	2.06	2.1	125	12.5	50	3.16	18692	22222	0.78	0.53	0.83	168.5	0.62	1.26	0.85	132	56
(14)	-	-	2.12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(15)	-	-	2.09	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(19)	2.25	2.08	2.14	160	10	60	3.13	18349	20833	0.98	0.68	0.94	141	0.91	1.07	0.75	140	60
(20)	2.21	2.06	2.11	150	15	60	3.5	17857	21739	0.76	0.56	0.83	147	0.69	1.1	0.73	173	73.6

a) $3g_{iso} = g_{\parallel} + 2g_{\perp}$ b) $3A_{iso} = A_{\parallel} + 2A$ c) $G = (g_{\parallel}-2)/(g_{\perp}-2)$



ESR spectrum of Cu(II) complex (13)

H. THERMALANALYSES(DTA AND TGA)

The thermal data of compounds **(14) and (21)** were presented in Table 6. The thermal curves in the 27-800°C temperature range indicated that, the compounds are thermally stable up to 40 °C. The weight losses recorded in the Co(II) compound **(14)** The endothermic peak observed at 135°C, with 3.1% weight loss (Calc. 3.19%) is due to loss of one coordinated water molecule. The endothermic peak observed at 155°C, with 3.2% weight loss (Calc. 3.3%) is due to loss of one coordinated water molecule. The endothermic peak observed at 200°C, with 11%weight loss (Calc. 11.19%) is due to loss of one coordinated acetate group, whereas, the loss of the other coordinated acetate group, was accompanied by an endothermic peak at 230°C with 12.6% weight loss (Calc. 12.45 %). The endothermic peak observed at 315°C, is corresponding to melting point of the compound. Finally, the compound showed several exothermic peaks at 420, 485, 510 and 530°C, with total 18.2% weight loss (Calc. 18.32%) corresponding to thermal decomposition with eventually formation of CoO molecule. The thermogram of Zn(II) compound **(21)** showed an endothermic peak at 45°C is due to broken of hydrogen bondings. The endothermic peak observed at 220°C, with 7.38% weight loss (Calc. 7.49%) was ascribed to loss of a coordinated acetate group. Another endothermic peak was observed at 230°C, with 8%weight loss (Calc. 8.1%), which is assigned to loss of coordinated acetate group. The endothermic peak observed at 305°C, is corresponding to the melting point of the compound. The compound showed several exothermic peaks at 370, 410 and 430, with total 11.97% weight loss (Calc. 12.15%) corresponding to thermal decomposition with the final formation of one ZnO molecule.

Table (6):- Thermal analyses for compounds (14) and (21).

Compound No. Molecular formula	Temp. (°C)	DTA (peak)		TGA (Wt.loss %)		Assignments
		Endo Found	Exo	Calc.		
Complex (14) $C_{14}H_{34}N_6O_{12}Co$	50	Endo	-	-	-	Broken of H-bondings
	135	Endo	-	3.19	3.1	Loss of (H_2O) coordinated water molecule
	155	Endo		3.3	3.2	Loss of (H_2O) coordinated water molecule
	200	Endo		11.19	11	Loss of coordinated (OAc) group
	230	Endo		12.6	12.45	Loss of coordinated (OAc) group
	315	Endo	-	-	-	Melting point
	420	-	Exo	18.32	18.2	Decomposition process with the formation of CoO
Complex (21) $C_{28}H_{56}N_{12}O_{22}Zn$	45	Endo	-	-	-	Broken of H-bondings
	220	Endo	-	7.49	7.38	Loss of coordinated (OAc) group
	230	Endo		8.10	8	Loss of coordinated (OAc) group
	305	Endo	-	-	-	Melting Point
	430	-	Exo	12.15	11.97	Decomposition process with the formation of ZnO

ANTIMICROBIAL ACTIVITY

In vitro biological screening tests of the compounds **(2), (3), (6), (7), (13), (19) and (21)** carried out as antibacterial and antifungal activity and presented in **(Table 7).** The antibacterial activity was tested against two bacterial strains; Gram-positive *Streptococcus aureus* (*S. aureus*) and *Bacillis subtilis* (*B. subtilis)* as well as Gram-negative *Escherichia coli (E.coli)* and *Salmonella sp. (S. sp.)* strains. The results compared with standard drug (Ampicllin (Gram positive) and Gentamicin (Gram negative). The data indicated that, the compound **(13)** were active against bacteria. antibacterial activitie against *Streptococcus aureus*, *Bacillis subtilis*, *Salmonella sp*. and *E.coli*. Also the results showed that, the order of cytotoxic effect against Gram positive and Gram negative strains for *Streptococcus aureus* is standard > **(13)> (3) > (2), (9) > (21) > (7).** The compound **(21)** also subjected to antifungal activity against *Aspergillus* fumigatus *(A.* fumigatus*)*. The compound **(7)** and compound (13) are also also subjected to antifungal activity against *Candida albicans*. Further, On comparing the results in general, it may be concluded that, the compound (13) have greater inhibiting power than the other compounds against all the microbes tested. The zone of inhibition was measured with respect to control.

Table(7): Biological activities of the compounds (2), (3), (6), (7), (13), (19) and (21) against bacteria and fungus.

Compounds	Inhibation zone in mm					
	S. aureus	*B. subtilis*	*S. SP.*	*E. coli*	*A. fumigatus*	*C. albicans*
Standard drug	23	32	17	19	23	25
DMSO	0	0	0	0	0	0
(2)	10	0	0	0	0	0
(3)	11	0	0	0	0	0
(6)	10	0	0	0	0	0
(7)	8	0	0	0	0	13
(13)	20	18	17	18	0	14
(19)	0	0	0	0	0	0
(21)	9	0	0	0	13	0

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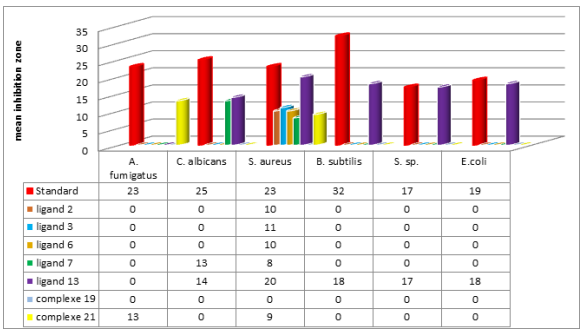


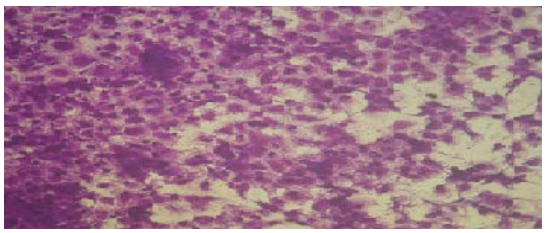
	A. fumigatus	C. albicans	S. aureus	B. subtilis	S. sp.	E.coli
Standard	23	25	23	32	17	19
ligand 2	0	0	10	0	0	0
ligand 3	0	0	11	0	0	0
ligand 6	0	0	10	0	0	0
ligand 7	0	13	8	0	0	0
ligand 13	0	14	20	18	17	18
complexe 19	0	0	0	0	0	0
complexe 21	13	0	9	0	0	0

Mean inhibition zone of the compounds (2), (3), (6), (7), (13), (19) and (21) against Aspergillus Funigatus, Streptococcs aureus, Bacillis Subtilis, Escherichia coli, Salmonella sp. and candida Albicans.

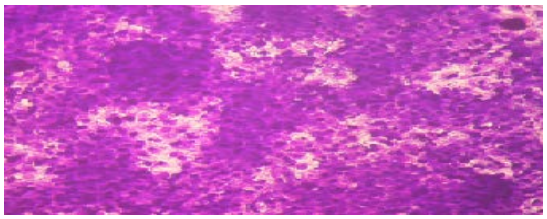
EVALUATION OF GLUTAMIC ACID DERIVATIVES AS ANTITUMOR

The antitumor effects of the compounds **(2), (3), (6), (7), (12), (13), (19) and (21)** in DMSO were evaluated against HepG-2 cell line. These were tested by comparing them with the standard drug (Sorafenib). The solvent DMSO showed no effect on cell growth as it reported previously. The compounds some of them shows interesting anticancer activity against HepG-2 cell line. The compound **(2)** show Inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = 124 µg/ml. Compound **(3)** show Weak inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = >500 µg/ml. Compound **(6)** Inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = 60.9 µg/ml. Compound **(7)** Inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = 20.1 µg/ml. Compound **(12)** Inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = 26.6 µg/ml. The compound **(13)** showed a Weak inhibitory activity against Hepatocellular carcinoma. cells was detected with IC_{50} = >500 µg/ml. Compound **(19)** showed Inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = 60.9 µg/ml. Compound **(21)** showed Inhibitory activity against Hepatocellular carcinoma cells was detected with IC_{50} = 7.24 µg/ml.

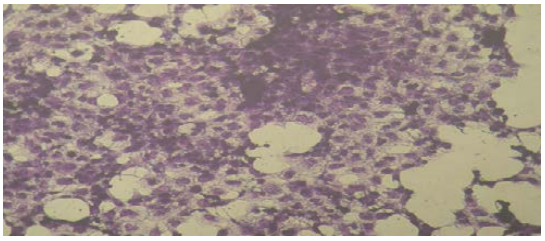
Standard drug



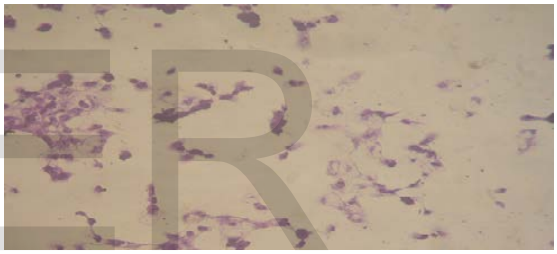
Compound 2 at 125 ug



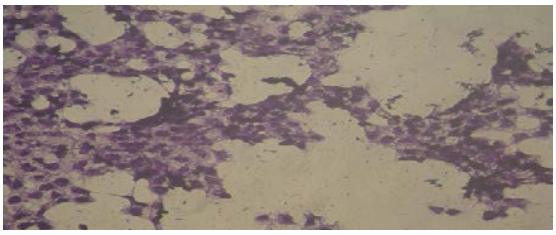
Compound 3 at 500 ug



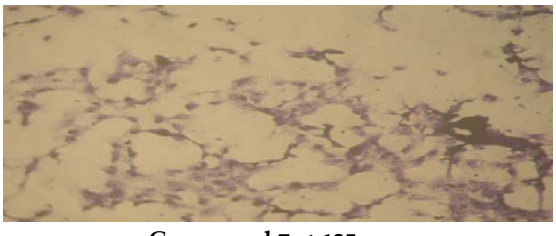
Compound 6 at 62.5 ug



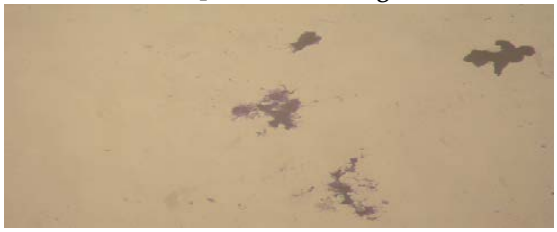
Compound 6 at 500 ug



Compound 7 at 15.6 ug



Compound 7 at 125 ug



Compound 7 at 500 ug

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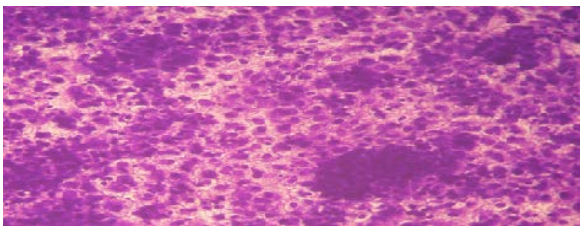
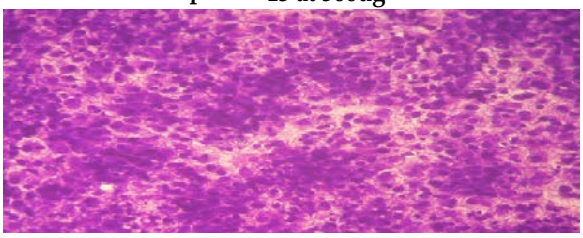
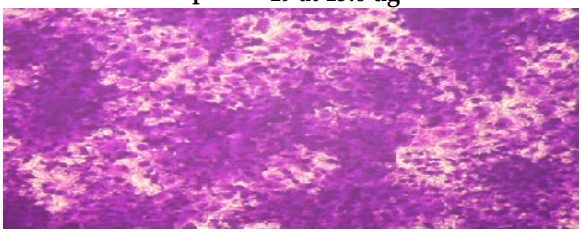


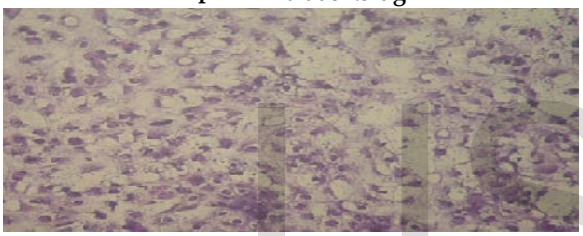
Compound 13 at 500ug



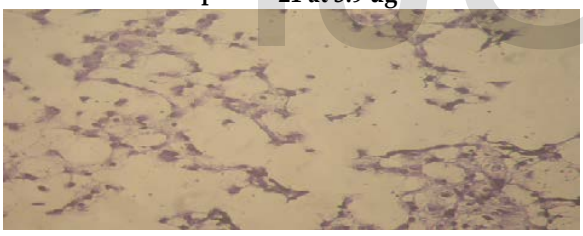
Compound 19 at 15.6 ug



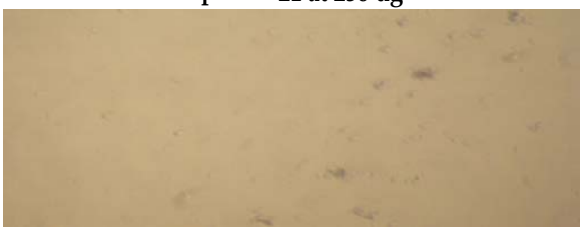
Compound 19 at 31.5 ug



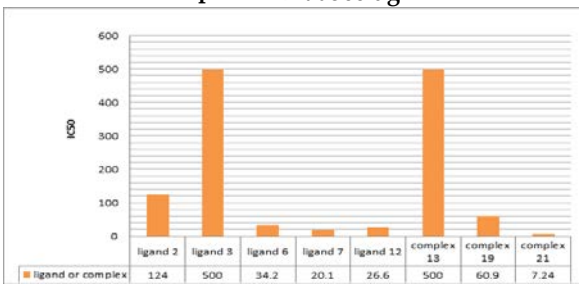
Compound 21 at 3.9 ug



Compound 21 at 250 ug



Compound 21 at 500 ug



IC_{50} values of (2), (3), (6), (7), (12),(13), (19) and (21) Against humanhepatocellular carcinoma cells (HepG2).

Conclusion

Spectroscopic (IR , UV-VIS, Mass, ^{1}H NMR, ^{13}C NMR and ESR spectra) and elemental studies of the compounds were reported. The magnetic properties and thermal analyses (DTA and TGA) were also carried out. The elemental analyses and mass spectral data have justified the composition of the compounds. The ESR spectra of compounds **(13), and (19),** showed an axial type (dx^2-y^2) ground state with a covalent bond character

The antimicrobial activity sowed that the compound **(13)** is more active agains *Salmonella sp., E.coli, Streptococcus aureus, Bacillis subtilis* and *C. albicans*. On comparing the results in general, it may be concluded that, the compound **(13)** have greater inhibiting power than the othe compounds against all the microbes tested.

The antitumor activity shwod that Some compounds **(2), (6), (7), (12) and (19),** showed inhibitory activity against hepatocellular carcinoma (HepG-2 cell line). The Zn(II) compound **(21)** showed a high potency of inhibition IC_{50} = 7.24 μg/ml.

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