

## Synthesis and Characterization of Schiff Base Folic Acid Based Ligand and Its Complexes

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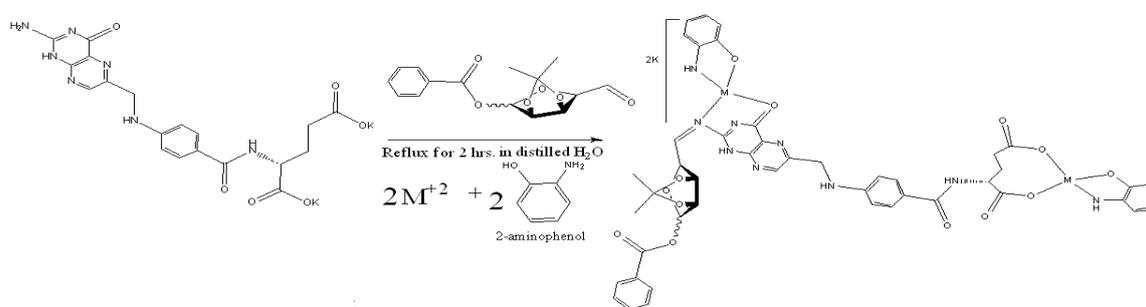
### Abstract

D-mannose sugar was used to prepare [benzoic acid 6-formyl-2,2-dimethyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl ester] (compound A). The condensation reaction of folic acid with (compound A) resulted in the formation of new ligand [L]. These compounds were characterized by elemental analysis CHN, atomic absorption A.A, (FT-I.R.), (U.V.-Vis), TLC, E.S. mass (for electrospray), molar conductance, and melting point. The new tetradentate ligand [L], reacted with two moles of some selected metal ions and two moles of (2-aminophenol), (metal : ligand : 2-aminophenol) at reflux in water medium to give a series of new complexes of the general formula  $K_2[M_2(L)(HA)_2]$  where  $M = Co^{(II)}, Ni^{(II)}, Cu^{(II)}$  and  $Cd^{(II)}$ . These complexes were characterized by elemental analyses [(C.H.N) and (A.A)], (FT-I.R), (U.V-Vis.), molar conductance,  $^1H, ^{13}C$ -NMR, TLC and magnetic moment measurements. From the above data the proposed geometry about  $Co^{(II)}, Ni^{(II)}, Cu^{(II)}$  and  $Cd^{(II)}$ , is tetrahedral structure. Biological activity of the ligand and its complexes was carried out on staphylococcus aureu, bacillus subtilis escherichia coli and psedomonas aeruginosa.

**Key Words:** vitamin B<sub>9</sub>,  $Cd^{(+2)}$  complexes infrared spectra , Schiff base,  $^1H, ^{13}C$ -NMR, TLC measurements.

## Introduction

Folic acid (pteroylglutamic acid) is heterocyclic compound which is composed of three large sub-components<sup>[1]</sup>. These are the pteridine ring, *para*-amino benzoic acid and glutamic acid. Glutamic acid is an amino acid that the body can actually synthesize by itself and is found in proteins, also known as vitamin M, vitamin B<sub>9</sub>,<sup>[2]</sup> vitamin B<sub>c</sub>.<sup>[3]</sup> Mixed-ligand complexes, play an important role in numerous chemical systems like water softening, ion exchange resin, electroplating, and dyeing<sup>[4-10]</sup>. The electrophilic carbon atoms of aldehydes and ketones can be targets of nucleophilic attack by amines. The end result of this reaction is a compound in which the C=O double bond is replaced by a C=N double bond. This type of compound is known as imines, or Schiff base<sup>[11]</sup>. In this work, we report the synthesis characterization and biological study of folic acid ligand and (compound A) with mixed ligand, and its complexes with selected transition elements, Scheme (1)



Where M=(Co<sup>II</sup>, Cu<sup>II</sup>, Ni<sup>II</sup>, and Cd<sup>I</sup>)

Scheme (1)

## Experimental

Reagents were purchased from Fluka and Redial – Dehenge Chemical Co. and used without further purification. FT-I.R spectra were recorded using THERMO SCIENTIFIC, ID5, ATR NICOLET, IS5 FT-IR spectrophotometer in the range (4000-400) cm<sup>-1</sup>. Electronic spectra of the prepared compounds were measured in the region (200-900) nm for 10<sup>-3</sup> M solutions in (DMSO) for the ligand and in distilled water for the complexes at 25°C using a Shimadzu160 spectrophotometer with 1.000±0.001 cm matched quartz cell. Elemental microanalyses were performed on a (C.H.N) analyzer model THERMO SCIENTIFIC FLASH 2000 ORGANIC ELEMENTAL ANALYZER. Metal content of the complexes were determined by atomic absorption (A.A) technique using a Shimadzu AA 680G atomic absorption spectrophotometer. Electrical conductivity measurements of the complexes were recorded at 25°C for 10<sup>-3</sup> M solutions of the samples in (DMSO) for the ligands and in distilled water for the complexes using a PW 9526 digital conductivity meter. Magnetic measurements were recorded on a Bruker BM6 instrument at 298°K following the Farady's method. Most of the measurements were made in Department of Chemistry, Manchester University, U.K

### Synthesis of [benzoic acid 6-formyl-2,2-dimethyl-tetrahydro-furo[3,4-d][1,3]dioxol-4-yl ester](A)

Compound A Fig.(1) , was prepared according to the following steps as in scheme (2).

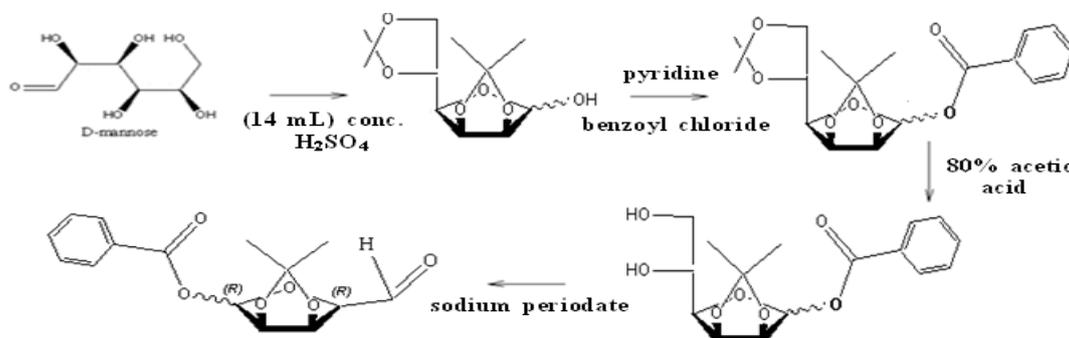
1) To a 1L of anhydrous acetone acidified with (14 mL) conc. H<sub>2</sub>SO<sub>4</sub> was added (20 g, 184.9 mmol) of D-mannose. The mixture was allowed to stir for 4-5 hrs., and a light yellow

solution was formed. This was neutralized with anhydrous  $\text{Na}_2\text{CO}_3$ , and then filtered off. Solution was removed under reduced pressure and a solid was formed. This was re-crystallized from toluene to yield white crystals (20 g, 90% yield), m.p.(120-122  $^\circ\text{C}$ ).

2) (6 g, 20.5 mmol) of compound (1) dissolved in (40 mL) of pyridine, then (5 mL) of benzoyl chloride was add to the stirred mixture that chilled in an ice bath. After (1 h.) of stirring, the solution was kept away from light for (24 h.) at room temperature and poured into vigorously stirred mixture of ice-water (25 mL). The mixture was stirred for (2 h.). Extracted with chloroform at room temperature (25  $^\circ\text{C}$ ) by using separating funnel to separate the chloroform layer (its density is higher than the water).Washing the layer with a solution of hydrochloric acid twice, and water separating layer, then washed with distilled water (25 ml), dried by anhydrous magnesium sulfate, stir for a quarter of an hour, filtered and evaporated white precipitate will be formed to give two crops of needles (2.8 g, 46.66 % yield), m.p (108  $^\circ\text{C}$ ).

3) A solution of (2 g ), (5.2 mmol) from compound 2 and 80% acetic acid (50 mL) was kept at room temperature with stirring for (48 h.). after which time the solution was concentrated, and white precipitate was formed. This was filtered off and then redissolved in butanol, dried and evaporated. A pale yellow product of diol (1.5 g, 75% yield), m.p. (100  $^\circ\text{C}$ ) was formed.

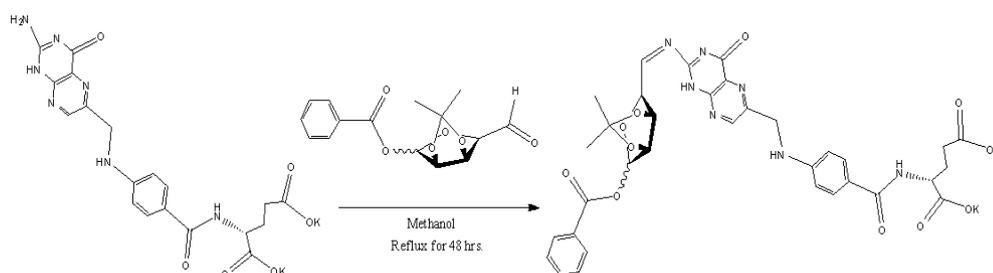
4) A solution of diol (2 g ), (6.1mmol) dissolved in a small amount of ethanol was added over (30 min) to the solution of sodium periodate (0.24 g ),(1.1 mmol) in  $\text{H}_2\text{O}$  (10 mL). The oxidation was allowed to proceed for (1 h.) at (0  $^\circ\text{C}$ ) and then white product was formed immediately which was allowed to cool for (1 h.) the solid was removed by filtration , and then dried by adding (20 mL) of ethyl acetate to give (0.9 g, 45% yield), m.p. (290 dec.  $^\circ\text{C}$ )



Scheme (2)

### Synthesis of the ligand [L]

To a solution of folic acid (2 g , 3.61 mmol) in methanol (20 ml)] was added to a mixture of KOH (0.25 g, 4.55 mmole), in (1 ml) of water and (compound A) (1.04 g , 3.56 mmole) dissolved in methanol (5 ml). The reaction mixture was allowed to reflux for (48 hr.), and then stirred at RT for (1 hr.). A mustard solid was formed which collected, by filtration, dried under vacuum for (24 hr.). Yield: (1g), (50 %) of the total compound. m.p (dec.250  $^\circ\text{C}$ ), according to the scheme (٢) .



Scheme (٣)

### Synthesis of the Complex

Synthesis of  $K_2[Co_2(L)(HA)_2]$  complex. A solution from [L] (0.172 g , 0.723 mmole) in a hot distilled water (20 ml), mixed with another solution of 2-aminophenol was (0.097 g , 9.7 mmole) in a hot distilled water (5 ml), was added slowly to a stirred solution of manganese(II) chloride tetrahydrate (0.176 g, 0.89 mmole) in (10 ml) distilled water. The resulting mixture was heated at refluxed for (2 hr.), during which, the solution became brown- yellow in color. The solution was concentrated by evaporating ethanol at room temperature and a deep-brown solid was formed. This was collected by filtration, dried under vacuum to give (0.23 g, 76.6 % yield), of the title compound, m.p (dec. 240 °C).

### Synthesis of $K_2[Ni_2(L)(HA)_2]$ , $K_2[Cu_2(L)(HA)_2]$ and $K_2[Cd_2(L)(HA)_2]$ Complexes

A similar method to that mentioned above was used to prepare the complexes of [L] with ( $Cd^{II}$ ,  $Ni^{II}$ , and  $Cu^{II}$ ). Fig.(1), and the same quantities of both of the ligand [L] and (2-aminophenole) were used. Table (1) stated the quantities, reaction conditions and physical properties of the prepared compounds.

## Results and Discussion

### Synthesis of the ligand[L]

The FT-I.R spectra of Fig.(2) show the five steps of forming (compound A). In the spectrum of folic acid Fig.(3) there are two sharp absorption bands at (3414 and 3547  $cm^{-1}$ ) due to the stretching vibration of  $\nu_{sy}(N-H)$  and  $\nu_{asy}(N-H)$  of the primary amine (R-NH<sub>2</sub>) group [12]. In the spectrum of (Compound A) Fig(4) there is a double bonds due to the carbonyl group  $\nu(C=O)$  stretching vibration at (1728 and 1631.7  $cm^{-1}$ )<sup>[13,14]</sup>. These bands were disappeared in the spectrum of the ligand [L]. Fig(5). Accompanied by the appearance of a new band at (1689.6  $cm^{-1}$ ) range assigned to the  $\nu(C=N)$  stretching indicates Schiff base reaction<sup>[15,16]</sup> Table (2). The (U.V-Vis) spectrum for the ligand [L], Fig.(11) exhibits a high intense absorption peak at (215 nm) (46511  $cm^{-1}$ ) ( $\epsilon_{max}= 700 \text{ molar}^{-1}.cm^{-1}$ ), (281 nm) (35587  $cm^{-1}$ ) ( $\epsilon_{max}= 688 \text{ molar}^{-1}.cm^{-1}$ ) assigned for ( $\pi \rightarrow \pi^*$ ) and a shoulder peak at (346 nm) (28901  $cm^{-1}$ ) ( $\epsilon_{max}= 182 \text{ molar}^{-1}.cm^{-1}$ ) assigned to ( $n \rightarrow \pi^*$ ) transition,<sup>[17,18]</sup> Table (3).

### Synthesis of the Complexes

The reaction of the ligand [L] with (2-aminophenol) and ( $Co^{II}$ ,  $Ni^{II}$ ,  $Cu^{II}$  and  $Cd^{II}$ ) was carried out in methanol under reflux. All complexes are stable in the solid state. The analytical and physical data, Table (1) and spectral data Table (2) are compatible with the suggested structures. In The FT-I.R spectra:- Band at (1689.6  $cm^{-1}$ ) that assigned to the  $\nu(C=N)$  stretching<sup>[15,16]</sup> of the spectrum of the ligand [L], Fig.(5) is shifted to lower frequency about (123  $cm^{-1}$ ) range compared with the spectra of the  $Co^{+2}$ ,  $Ni^{+2}$ ,  $Cu^{+2}$ , and  $Cd^{+2}$  complexes due

to the forming ring system with the metal ions and delocalization of electron  $\pi$  density. The spectrum of [L] Fig.(5), shows sharp band at ( $1724\text{ cm}^{-1}$ ) due to the  $\nu(\text{C}=\text{O})$  stretching<sup>[13,14]</sup> this band is shifted to lower frequency because of the coordination with the metal ions. Metal oxygen and metal nitrogen band further confirmed by the presence of peaks at ( $582\text{-}584\text{ cm}^{-1}$ ) and ( $425\text{-}480\text{ cm}^{-1}$ ) range were assigned to  $\nu(\text{M-O})$ , and  $\nu(\text{M-N})$ , stretches for the  $\text{Ni}^{+2}$ ,  $\text{Co}^{+2}$ ,  $\text{Cu}^{+2}$  and  $\text{Cd}^{+2}$  complexes, respectively. Table (2). The (U.V-Vis.) Spectra:- Figs.(12), (13), (14) and (15) display the (U.V- Vis) spectra of the  $\text{Co}^{+2}$ ,  $\text{Ni}^{+2}$ ,  $\text{Cu}^{+2}$ , and  $\text{Cd}^{+2}$  complexes, respectively. Table (3) summarized the absorption peaks of the complexes In each case the spectrum showed two intense peaks in the (U.V) region at ( $283\text{-}247\text{ nm}$ ) assigned to the ligand field<sup>[19]</sup>. The spectra of ( $\text{Co}^{+2}$ ), ( $\text{Ni}^{+2}$ ) and ( $\text{Cu}^{+2}$ ) complexes Figs.(12,13 and 14) exhibited strong peaks at visible region at: ( $500\text{ nm}$ ) ( $20000\text{ cm}^{-1}$ ) ( $\epsilon_{\text{max}} = 30\text{ molar}^{-1}\cdot\text{cm}^{-1}$ ), ( $490\text{ nm}$ ) ( $20408\text{ cm}^{-1}$ ), ( $\epsilon_{\text{max}} = 550\text{ molar}^{-1}\cdot\text{cm}^{-1}$ ) and ( $530\text{ nm}$ ) ( $18867\text{ cm}^{-1}$ ), ( $\epsilon_{\text{max}} = 100\text{ molar}^{-1}\cdot\text{cm}^{-1}$ ) assigned to ( ${}^4A_2 \rightarrow {}^4T_{1(g)}$ ), ( $T_1 \rightarrow {}^1T_{2(p)}$ ), ( ${}^2T_2 \rightarrow T_v$ ) (d-d) transitions respectively suggesting tetrahedral structures<sup>[20]</sup> around ( $\text{Co}^{+2}$ ), ( $\text{Ni}^{+2}$ ) and ( $\text{Cu}^{+2}$ ). The strong peak at visible region ( $410\text{ nm}$ ) ( $24390\text{ cm}^{-1}$ ) ( $\epsilon_{\text{max}} = 600\text{ molar}^{-1}\cdot\text{cm}^{-1}$ ) in the Cd- complex is assigned to charge transfer transition confirming tetrahedral structure around  $\text{Cd}^{\text{II}}$  ion<sup>[21]</sup> Fig.(15). The molar conductance: - The observed molar conductance value measured in (DMSO) ( $10^{-3}\text{ M}$  solution) at room temperature lies in the ( $70\text{-}80\text{ S}\cdot\text{cm}^2\cdot\text{mole}^{-1}$ ) range, indicating their electrolytic nature with (1:2) ratio of the complexes<sup>[22,23]</sup>. Table (3). The magnetic moment The magnetic moments values of the  $\text{K}_2[\text{Ni}_2(\text{L})(\text{HA})_2]$  complexes are shown in Table (3-30). The value of  $\mu_{\text{eff}}$  lies in ( $2.83\text{ B. M.}$ ) of the complexes indicating paramagnetic properties and tetrahedral geometry around ( $\text{Ni}^{+2}$ ) ion.<sup>[24]</sup>

### **${}^1\text{H-NMR}$ Spectrum of $\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$ Complex**

The  ${}^1\text{H-NMR}$  spectrum for  $\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$  complex in  $\text{DMSO-d}_6$  Fig.(1٦) showed peak at ( $\delta 1.45\text{ ppm-CH}$ )(6H) attributed to two methyl groups. The quartet signal obtained at ( $\delta 2.10\text{ ppm-CH}$ )(4H) due to methylene  $\text{CH}_2$  group. The doublet signal obtained at ( $\delta 2.30\text{ ppm-CH}$ )(3H) due to methylene  $\text{CH}_2$  group is shifted to low field as a result of the effect of  $\text{C}=\text{O}$  group. Another doublet signal obtained at ( $\delta 4.40\text{ ppm-CH}$ )(1H) is due to methylene  $\text{CH}_2$  group is shifted to low field because of the cycle effect from one side and N-H group effect of the other side. A signal at ( $\delta 4.0\text{ ppm}$ )(1H) assigned to (NH) aromatic. The triplet signal at ( $\delta 4.5\text{ ppm-CH}$ )(3H) assigned to methane (CH) group. This group has shifted to low field as a result of the effect of (NH sec.) amide group. Two triplet signals assigned to CH group of tetrahydrofuran, the first at ( $\delta 4.2\text{ ppm-CH}$ )(3H), and the second at ( $\delta 6.7\text{ ppm-CH}$ )(3H) is shifted to low field-high frequency as a consequence of the effect of C-O group. Another two triplet signals observed, due to the 1,3-dioxan. The first at ( $\delta 4.3\text{ ppm-CH}$ )(4H). The second signal at ( $\delta 4.9\text{ ppm-CH}$ )(4H) is shifted to low field-high frequency because of the effect of C-O group. The doublet signal at ( $7.6\text{ ppm-CH}$ )(2H) due to aldimine group. A single signal at ( $\delta 8.2\text{ ppm-CH}$ )(1H) due to ( $-\text{CH}=\text{N}$ ) pyrazine group. A single signal at ( $\delta 8.3\text{ ppm-NH}$ )(1H) due to (NH) amide group. And multiple group of resonance signals at ( $\delta 7.2\text{-}8.8\text{ ppm-CH}$ ) range due to benzene ring. The NMR spectral data of  $\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$  complex was compared with the spectral data for the ligand according to chemoffes program..Table (4) summarized the details of the chemical shifts.

### **${}^{13}\text{C-NMR}$ Spectrum of $\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$ Complex**

The  ${}^{13}\text{C-NMR}$  spectrum of the  $\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$  complex in  $\text{DMSO-d}_6$  solvent is shown in Fig.(١٧). The characterized resonances are listed in Table (5).

### E.S-mass Spectrum of (Compound A)

The E.S-mass (+) spectrum of compound (A), Fig.(١٨) shows the parent ion peak at ( $M/Z=292.09$ ), which corresponds to  $(M)^+$ , other fragments are summarized in Table (6). Peak detected at  $[M/Z=315.1$  is assigned for  $(M+Na)^+$

### E.S-mass Spectrum of ligand [L]

The E.S-mass (+) spectrum of derivative ligand [L]. Fig.(١٩), shows the parent ion peak at ( $M/Z=791.14$ ), which corresponds to  $(M)^+$ , other fragments are summarized in Table (7). Peak detected at  $[M/Z=814.5$  is assigned for  $(M+Na)^+$

### Biological Activity for the ligand (L) and its Complexes

The biological activity for the ligand (L) and its complexes were studied using inhibition method [25-28]. Four types of pathogenic bacteria two were gram positive which are Staphylococcus aureus and Bacillus subtilis, the second two were gram negative which are Escherichiacoli and Pseudomonasaeruginosa. The ligand (L), did not show any inhibition diameter against any type of the four bacterial, neither after 24 hrs. nor after 48 hrs., Table (8). However complexes show more activity than the ligand under similar experimental conditions with the same kinds of bacteria.

### Thin-Layer Chromatography (TLC) Measurement

The T.L.C technique measurement for the derivative ligand (L) was performed with  $Co^{+2}$ ,  $Ni^{+2}$ ,  $Cu^{+2}$ , and  $Cd^{+2}$  complexes and resulted the appearance of a new spots in different positions belong to  $Co^{+2}$ ,  $Ni^{+2}$ ,  $Cu^{+2}$ , and  $Cd^{+2}$  ion complexes this spots position are differs from the position of the starting materials spots about (4.8 mm) range indicating the forming of new compounds.

### The Proposed Molecular Structure

The proposed molecular structure of  $K_2[Ni_2(L)(HA)_2]$  complex according to chemoffice program displays the bond angles and bond length Table (9) and the proposed geometrical shape of the complex is tetrahedral Fig.(٢٠).

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**Table No. (1): The physical properties of [L] and its complexes.**

Compound	M.W	Yield %	w.t of metal Ion= mmole	m.p°C	Color	Found, (Cal.) %				
						C	H	N	K	metal
(Compound A)	292.28	45	-	290 Dec.	Yellow And white	(61.64) 60.41	(5.52) 5.00	(32.84) 32.11	-	-
[L]	791.85	50	-	250	Deep Mustered	(51.47) 50.70	(3.82) 3.11	(12.40) 11.20	(9.89) 9.00	-
K <sub>2</sub> [Co <sub>2</sub> (L)(HA) <sub>2</sub> ]	1083.83	60	0.756	270 Dec.	Pale Brown	(50.98) 50.33	(3.72) 3.21	(11.63) 11.03	(3.61) 3.11	(10.88) 9.01
K <sub>2</sub> [Cu <sub>2</sub> (L)(HA) <sub>2</sub> ]	1093.05	70	0.757	240 Dec.	Pale-Brown	(50.55) 43.88	(3.69) 3.01	(11.53) 9.78	(3.58) 3.00	(11.36) 9.55
K <sub>2</sub> [Ni <sub>2</sub> (L)(HA) <sub>2</sub> ]	1083.35	63	0.753	230 Dec.	Green	(51.00) 48.17	(3.72) 2.52	(11.64) 9.01	(3.61) 2.01	(10.48) 9.00
K <sub>2</sub> [Cd <sub>2</sub> (L)(HA) <sub>2</sub> ]	1190.78	76	0.755	260 Dec.	Brown	(46.40) 44.90	(3.39) 2.42	(10.59) 8.00	(3.28) 2.60	(18.88) 16.65

(Calcu.): calculated

(dec.): decomposed

**Table No. (2): The FT-I.R spectral data(wave number)cm<sup>-1</sup> of [L] and its complexes**

Compound	$\nu$ (N-H) primary R-NH <sub>2</sub>	$\nu$ (N-H) Secondary R <sub>2</sub> -NH	$\nu$ (O-H)	$\nu$ (COO) <sup>-</sup> as $\nu$ (COO) <sup>-</sup> s	$\nu$ (C=N)imine	$\nu$ (CH <sub>3</sub> )	$\nu$ (C-N)aroma $\nu$ (C-N)aliph.	M-O M-N
[compound A] [L]	-	3344(br)	-	1724(sh) 1558(sh) 1444.6(sh)	1689.6(sh)	1350(sh)	1396(sh) 1288(sh)	-
2-aminophenole	3475(sh) 3305(sh)	-	3051(br)	-	-	-	1217(sh)	-
K <sub>2</sub> [Co <sub>2</sub> (L)(HA) <sub>2</sub> ]	-	3332.9(sh)	-	1602.8(sh) 1514(sh) 1404(sh)	1573.9(sh)	1320(sh)	1317(sh) 1273(sh)	584(sh) 425(sh)
K <sub>2</sub> [Ni <sub>2</sub> (L)(HA) <sub>2</sub> ]	-	3310(sh)	-	1602.8(sh) 1514(sh) 1404(br)	1573.9(sh)	1300(sh)	1317(sh) 1273(sh)	584(sh) 430(sh)
K <sub>2</sub> [Cu <sub>2</sub> (L)(HA) <sub>2</sub> ]	-	3319(sh)	-	1593(sh) 1539(br) 1396(s)	1577.7(sh)	1325(sh)	1350(w) 1276.8(br)	582.5(sh) 480(sh)
K <sub>2</sub> [Cd <sub>2</sub> (L)(HA) <sub>2</sub> ]	-	3332.9(br)	-	1604.7(sh) 1541(br) 1409.9(br)	1573.9(s)	1330(sh)	1349(w) 1273(sh)	584(sh) 460(sh)

S: strong vs: very strong m: medium w: weak  
arom: aromatics,sh: strong sharp br: broad o.o.p: out of plane aliph: ali phatic  
 $\nu$ : stretching  $\delta$ : bending

**Table No. (3): Electronic spectral data and conductance measurements of the ligand and complexes.**

Compound	$\lambda$ nm	$\nu$ $\text{cm}^{-1}$	$\epsilon_{\text{max}}$ molar $^{-1}$ . $\text{cm}^{-1}$	Assignment	M.C*(ohm $^{-1}$ .c m $^2$ .mole $^{-1}$ )	Geometrical shape	Solvent	Ratio
[L]	215	46511	700	$\pi \rightarrow \pi^*$	-	-	-	-
	281	35587	688	$n \rightarrow \pi^*$				
	346	28901	182	$n \rightarrow \pi^*$				
$\text{K}_2[\text{Co}_2(\text{L})(\text{HA})_2]$	٢٨٣	٣٥٣٣٥	٣٥٠	Ligand field	77	Tetrahedral	DMSO	1:2
	418	23923	401	${}^4A_2 \rightarrow {}^4T_{1(F)}$				
	436	22935	416	${}^4A_2 \rightarrow {}^4T_{1(F)}$				
	500	20000	30	${}^4A_2 \rightarrow {}^4T_{1(F)}$				
$\text{K}_2[\text{Ni}_2(\text{L})(\text{HA})_2]$	247	40485	2421	Ligand field	76	Tetrahedral	DMSO	1:2
	418	23923	457	${}^3T_1 \rightarrow {}^1T_2$				
	436	22935	474	${}^3T_1 \rightarrow {}^1T_{2(P)}$				
	490	20408	550	${}^3T_1 \rightarrow {}^1T_{2(P)}$				
$\text{K}_2[\text{Cu}_2(\text{L})(\text{HA})_2]$	254	39370	2452	Ligand field	80	Tetrahedral	DMSO	1:2
	420	238092	400	${}^2T_2 \rightarrow {}^2T_6$				
	437	22883	433	${}^2T_2 \rightarrow {}^2T_6$				
	530	18867	100	${}^2T_2 \rightarrow {}^2T_7$				
$\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$	٢٧٠	٣٧٠٣٧	٥٥	Ligand field	70	Tetrahedral	DMSO	1:2
	410	24390	600	<i>Ch.T</i>				

**Table No. (4):  ${}^1\text{H-NMR}$  Spectral data of  $\text{K}_2[\text{Cd}_2(\text{L})(\text{HA})_2]$** 

Group	H	$\delta$ ppm
Methane	$\text{C}_{(37)}\text{-H}$	4.5
1,3-dioxolan	$\text{C}_{(9,10)}\text{-H}$	4.3-4.9
Tetrahydrofuran	$\text{C}_{(11,8)}\text{-H}$	4.2,6.7
1-benzene	$\text{C}_{(1,2,3,4,\dots)}\text{-H}$	7.2-8.8
Aldimine	$\text{C}_{(7)}\text{-H}$	7.6
2-pyrazine	$\text{C}_{(26)}\text{-H}$	8.2
Methylene	$\text{C}_{(38,39,28)}\text{-H}_2$	2.10, 2.30, 4.40
Methyl	$\text{C}_{(13,14)}\text{-H}_3$	1.45
Aromatic C-NH	$\text{C}_{(23)}\text{-NH}$	4.0
Amide	$\text{C}_{(39)}\text{-NH}$	8.3
DMSO solvent		2.5

**Table No. (5):<sup>13</sup>C-NMR Spectral data of K<sub>2</sub>[Cd<sub>2</sub>(L)(HA)<sub>2</sub>]**

Group	C <sup>13</sup>	δ ppm
Aliphatic	C <sub>(١٧)</sub>	1٢٥
Pyrimidine	C <sub>(25,22)</sub>	17٥, ١٧٧
Benzen	C <sub>(1,6,19,29.....)</sub>	148,120,147,132,131
Pyrazine	C <sub>(23,27,24)</sub>	145, 149,150, 146
Amide	C <sub>(35)</sub>	169
Carboxyl	C <sub>(36,40)</sub>	177,167
DMSO solvent		29
Imine	CH <sub>(7)</sub>	164
Benzen	CH <sub>(2,5,15,17.....)</sub>	123,113,127,109,116,126,129,132,104
Tetrahydrofuran	CH <sub>(11,10,9,8)</sub>	78,92,73,95
Aliphatic	CH <sub>(37)</sub>	57
Pyrazine	CH <sub>(26)</sub>	144
Aliphatic	CH <sub>2</sub> <sub>(28,38,39)</sub>	24,26
Aliphatic	CH <sub>3</sub> <sub>(13,14)</sub>	23

**Table No. (6):E.S-mass spectral data of (compound A).**

Fragment Ions	Mass/charge (m/z)	Relative abundance
[M] <sup>+</sup>	292.09	30
[M-{COH }] <sup>+</sup>	264.2	15
[M-{ COH-CH <sub>2</sub> }] <sup>+</sup>	250.2	55
[M-{ COH-CH <sub>2</sub> -CH <sub>2</sub> }] <sup>+</sup>	236.0	32
[M-{ COH-CH <sub>2</sub> -CH <sub>2</sub> - C <sub>3</sub> H <sub>7</sub> O <sub>3</sub> }] <sup>+</sup>	121.0	62

**Table No. (7):E.S-mass spectral data of [L].**

Fragmentations	Mass/chr-ge (m/z)	Relative abundance
[M] <sup>+</sup>	791.14	22
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> }] <sup>+</sup>	671.11	20
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> }] <sup>+</sup>	575.2	18
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> -C <sub>6</sub> H <sub>8</sub> O <sub>3</sub> }] <sup>+</sup>	447.0	25
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> -C <sub>6</sub> H <sub>8</sub> O <sub>3</sub> -C <sub>2</sub> H <sub>3</sub> N}] <sup>+</sup>	406.08	21
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> -C <sub>6</sub> H <sub>8</sub> O <sub>3</sub> -C <sub>2</sub> H <sub>3</sub> N -C <sub>5</sub> N <sub>4</sub> O}] <sup>+</sup>	274.0	8
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> -C <sub>6</sub> H <sub>8</sub> O <sub>3</sub> -C <sub>2</sub> H <sub>3</sub> N -C <sub>5</sub> N <sub>4</sub> O -C <sub>2</sub> H <sub>5</sub> N}] <sup>+</sup>	231.0	32
[M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> -C <sub>6</sub> H <sub>8</sub> O <sub>3</sub> -C <sub>2</sub> H <sub>3</sub> N -C <sub>5</sub> N <sub>4</sub> O -C <sub>2</sub> H <sub>5</sub> N-C <sub>3</sub> H <sub>2</sub> }] <sup>+</sup>	169.0	40
M-{C <sub>7</sub> H <sub>4</sub> O <sub>2</sub> -C <sub>2</sub> HKO <sub>2</sub> -C <sub>6</sub> H <sub>8</sub> O <sub>3</sub> -C <sub>2</sub> H <sub>3</sub> N -C <sub>5</sub> N <sub>4</sub> O -C <sub>2</sub> H <sub>5</sub> N-C <sub>3</sub> H <sub>2</sub> -C <sub>2</sub> H <sub>3</sub> NO }] <sup>+</sup>	111.9	19

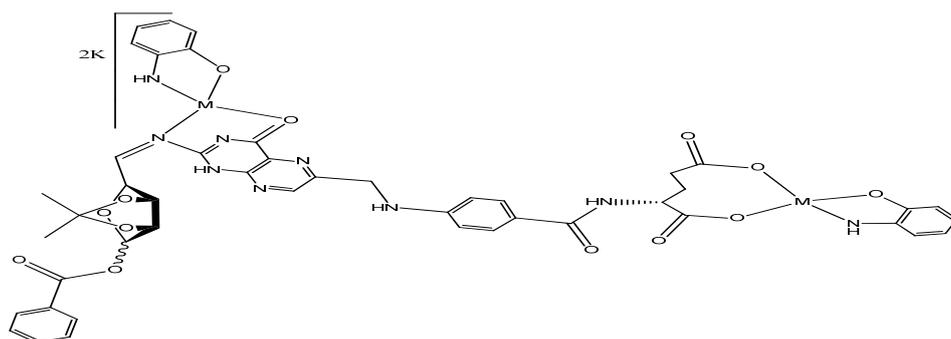
**Table No. (8):Inhibition circle diameter in millimeter for(compoundA),ligand[L] and complexes after 24 hrs.,and after 48 hrs.**

Compounds	<i>Staphylococcus aureu</i>		<i>Pseudomonas aeruginosa</i>		<i>Bacillus subtilis</i>		<i>Escherichia coli</i>	
	24 hrs.	48 hrs.	24 hrs.	48 hrs.	24 hrs.	48 hrs.	24 hrs.	48 hrs.
(Compound A) and [L]	0	0	0	0	0	0	0	0
K <sub>2</sub> [Co <sub>2</sub> (L <sub>(3)</sub> )(HA) <sub>2</sub> ]	20	22	·	·	18	17	18	18
K <sub>2</sub> [Ni <sub>2</sub> (L <sub>(3)</sub> )(HA) <sub>2</sub> ]	20	19	12	12	17	18	10	10
K <sub>2</sub> [Cu <sub>2</sub> (L <sub>(3)</sub> )(HA) <sub>2</sub> ]	15	17	·	10	15	15	17	16
K <sub>2</sub> [Cd <sub>2</sub> (L <sub>(3)</sub> )(HA) <sub>2</sub> ]	20	24	15	16	18	19	14	13

**Table No.(9):The propped bond lengths and bond angles of K<sub>2</sub>[Cd<sub>2</sub>(L)(H A)<sub>2</sub>]complex.**

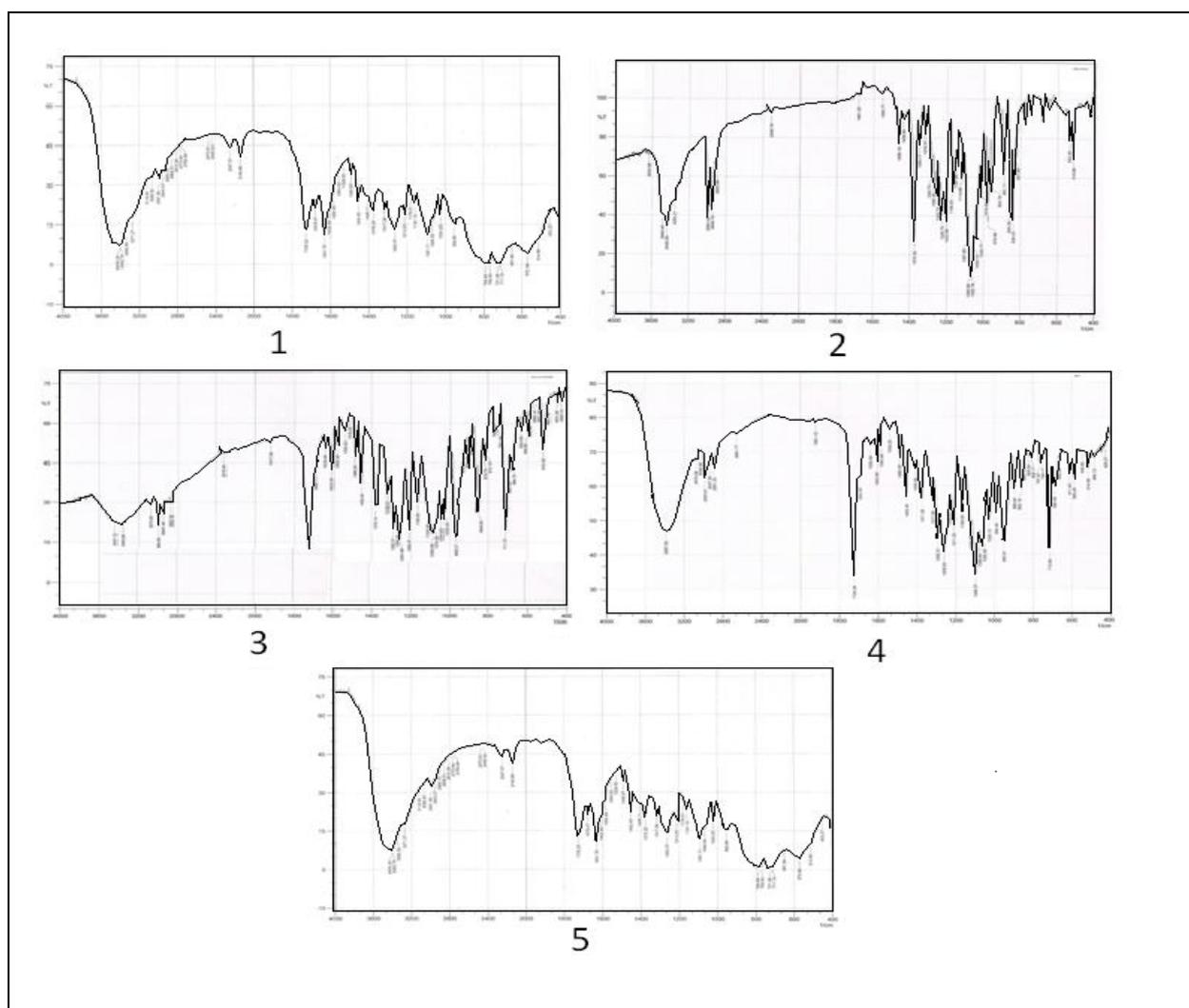
Type of bond	Bond length (A°)	Type of angles	Bond length (A°)
Ni-O	1.790	O-Ni-O	180.000
Ni-N	4.434	O-Ni-N	77.183
N-H	1.050	Ni-O-C	109.500
C-H	1.100	H-N-Ni	126.702
C-N	1.260	N-Ni-N	158.914
C-C	1.395	Ni-N-C	52.614
C-O	1.208		

(A°)= Angstrom,, (°)= degree



Where  $M=(\text{Co}^{\text{II}}, \text{Cu}^{\text{II}}, \text{Ni}^{\text{II}}, \text{and } \text{Cd}^{\text{I}})$

**Figure No. (1): formation of complexes**



**Figure No.(2) : The I.R. spectra of the four steps of forming (compound A)**

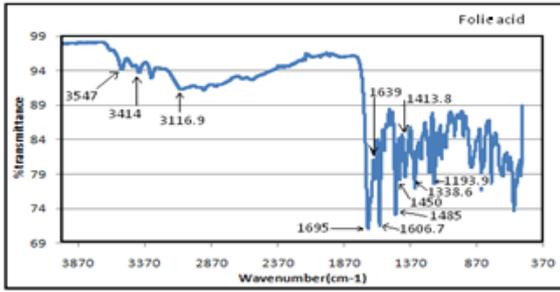


Fig. (3) Infrared Spectrum of folic acid

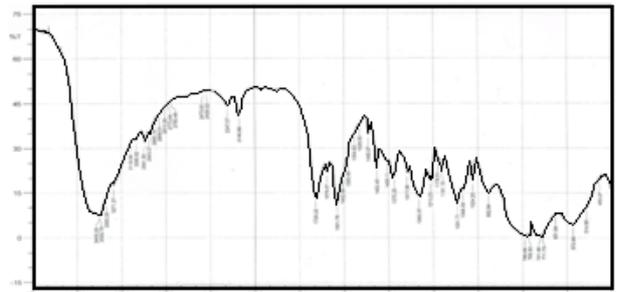


Fig. (4) Infrared Spectrum of compound A

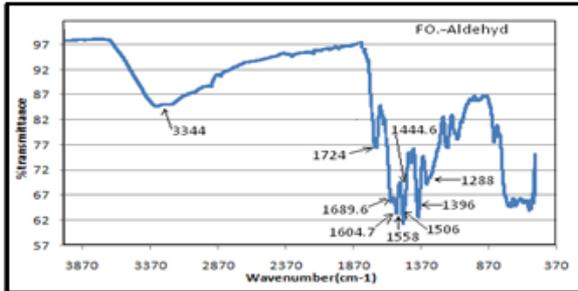


Fig. (5) I.R. Spectrum of derivative ligand [L]

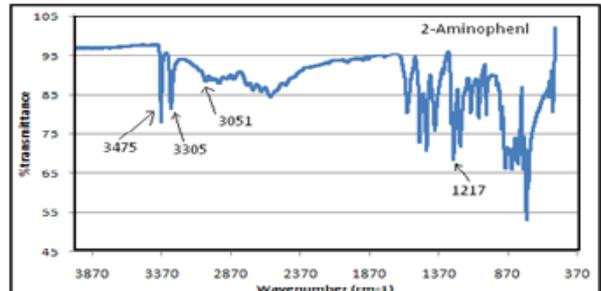


Fig. (6) I.R. Spectrum of 2-Aminophenol

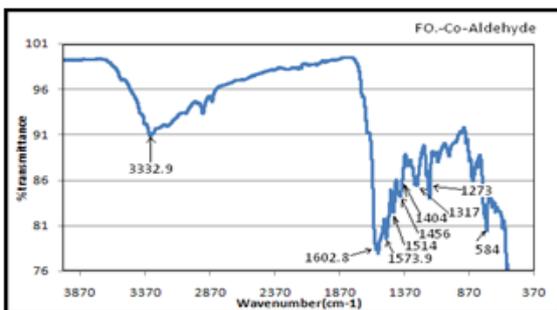


Figure ( 7 ) I.R. spectrum of  $K_2 [Co_2(L)(HA)_2]$  complex

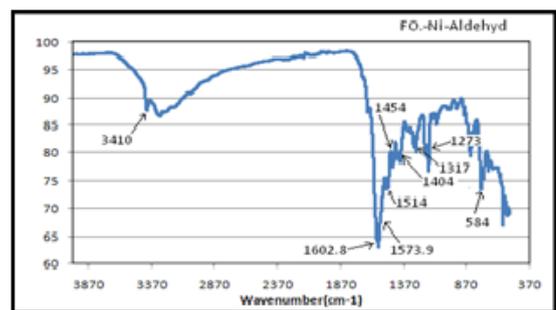


Figure ( 8 ) I.R. spectrum of  $K_2 [Ni_2(L)(HA)_2]$  complex

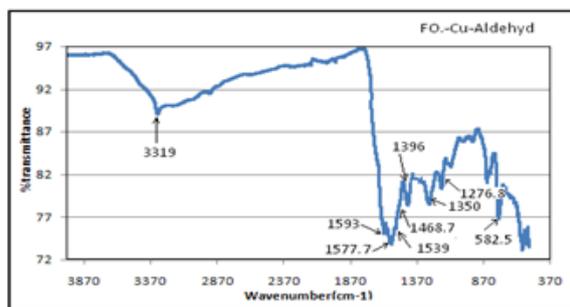


Figure ( 9 ) I.R. spectrum of  $K_2 [Cu_2(L)(HA)_2]$  complex

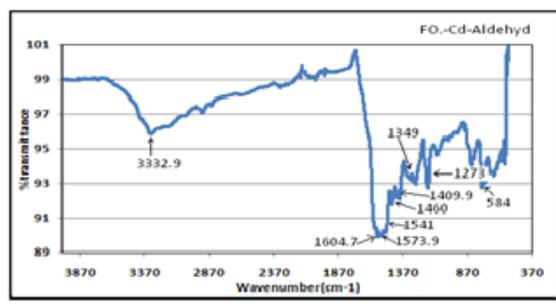


Figure (10) Infrared spectrum of  $K_2 [Cd_2(L)(HA)_2]$  complex

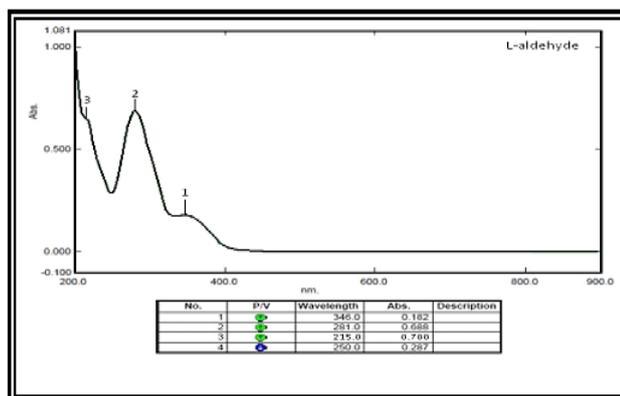


Figure ( 11 ) The U.V-Vis Spectrum of derivative ligand [L]

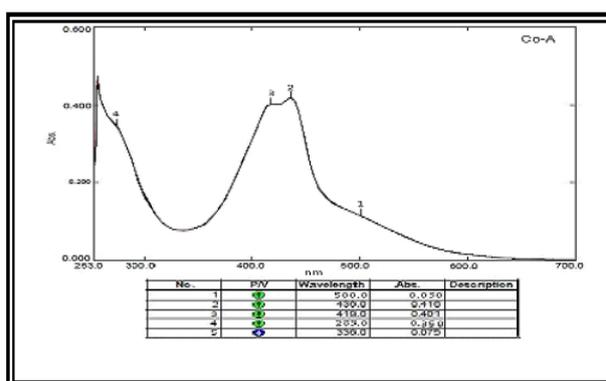


Figure ( 12 ) The U.V-Vis Spectrum of  $K_2[Co_2(L)(HA)_2]$  complex

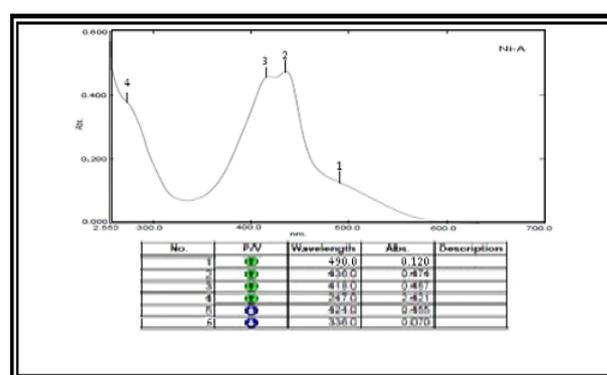


Figure ( 13 ) The U.V-Vis Spectrum of  $K_2[Ni_2(L)(HA)_2]$  complex

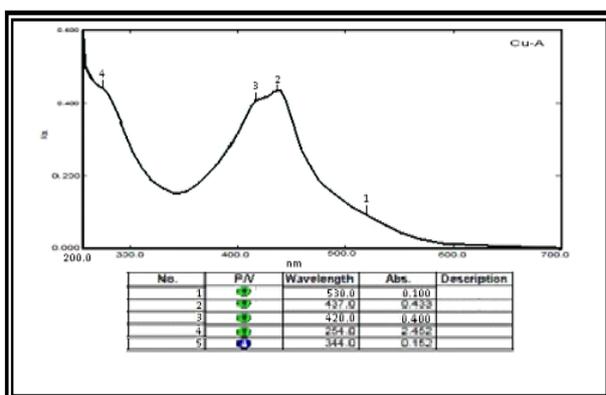


Figure ( 14 ) The U.V-Vis Spectrum of  $K_2[Cu_2(L)(HA)_2]$  complex

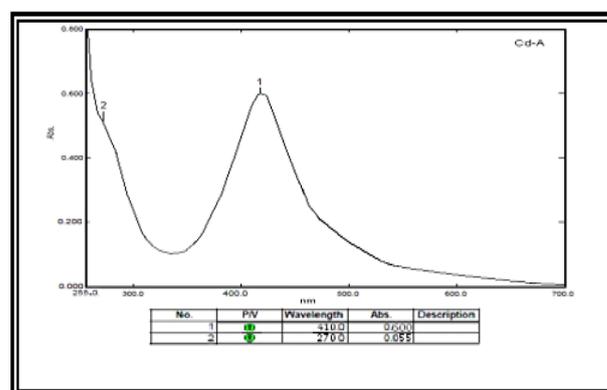


Figure ( 15 ) The U.V-Vis Spectrum of  $K_2[Cd_2(L)(HA)_2]$  complex

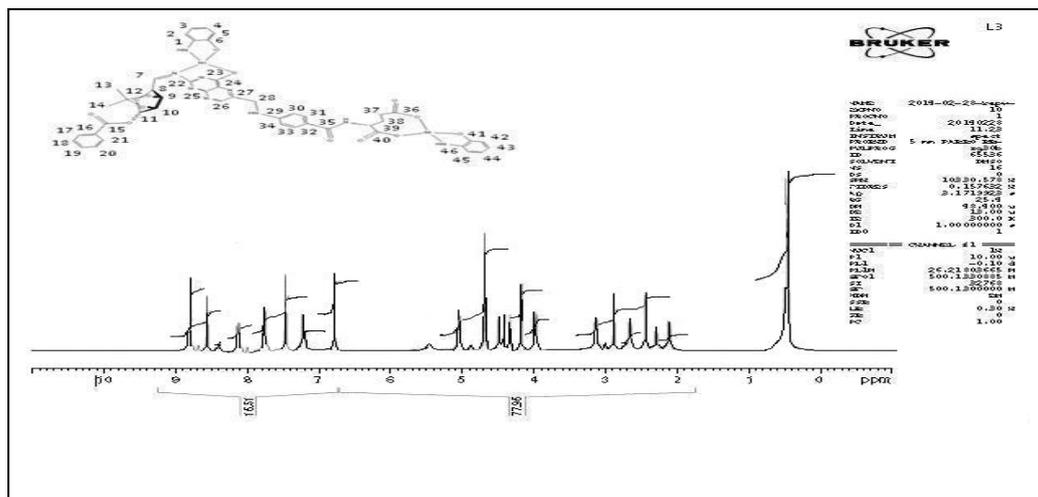


Figure No. (١٦): <sup>1</sup>H-NMR Spectral data of K<sub>2</sub>[Cd<sub>2</sub>(L)(HA)<sub>2</sub>]complex

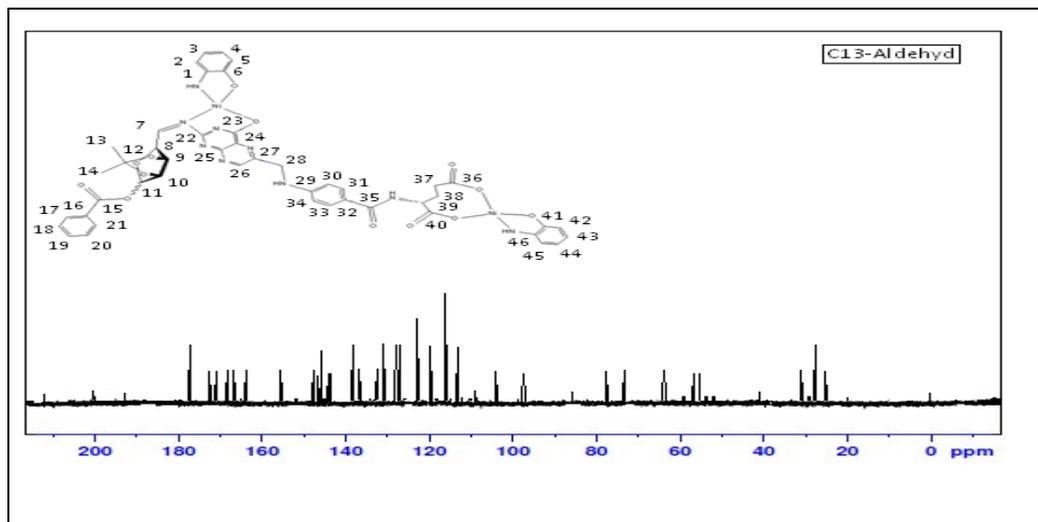


Figure No. (١٧): <sup>13</sup>C-NMR of K<sub>2</sub>[Cd<sub>2</sub>(L)(HA)<sub>2</sub>]complex.

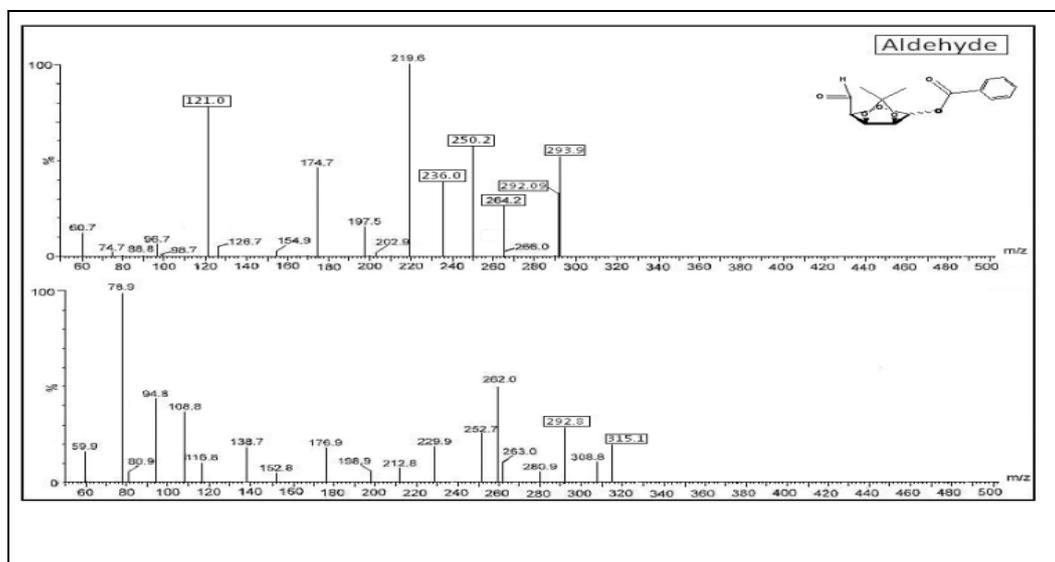


Figure No. (١٨): E.S-mass spectrum of the starting material (compound A)

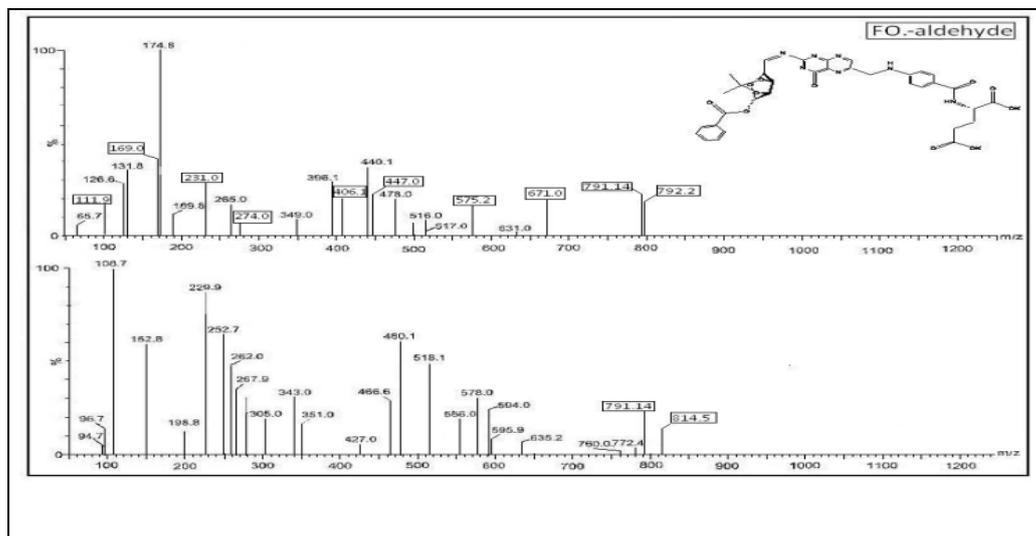
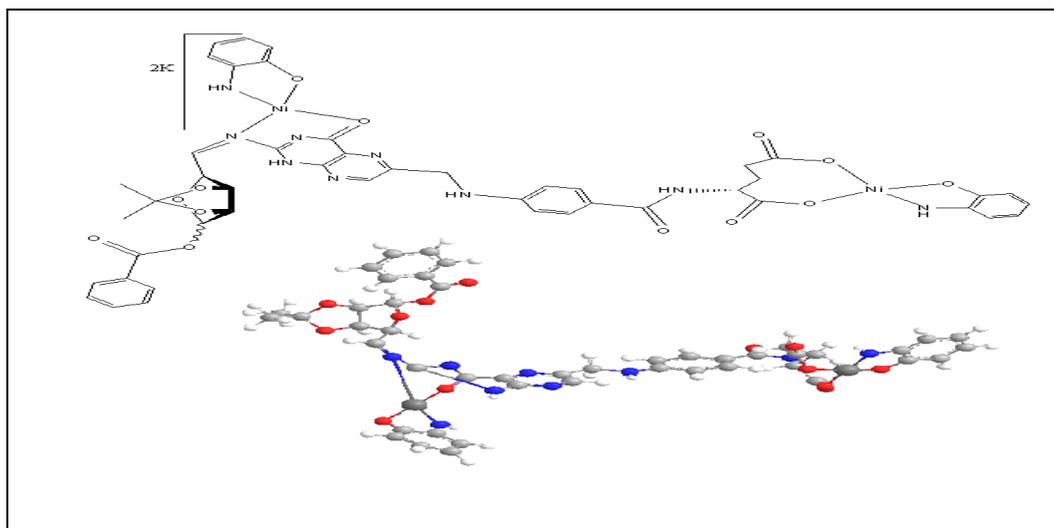


Figure No. (١٩): E.S-mass spectrum of derivative ligand [L].

Figure No. (2٠) :The proposed molecular structure of  $K_2[Ni_2(L)(HA)_2]$  complex

## تحضير وتشخيص قاعدة شف لحمض الفوليك كليكاند ومعداته

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استلم البحث في: ١٥ تشرين الاول ٢٠١٤ , قبل البحث في ٢ شباط ٢٠١٥

### الخلاصة

تضمن البحث تحضير مركب يعتبر كمادة اولية وليكاندا مشتقا من حامض الفوليك بطريقة قاعدة شف مع سلسلة جديدة من المعقدات (المتشكلة من مزيج من الليكاندات) بوجود هيدروكسيد البوتاسيوم والميثانول وسطا للتفاعل باشكال رباعية السن حيث تم اضافة سكر الذي مانوس الى لتر واحد من الاسيتون المحمض بحامض الكبريتيك المركز ثم يذاب الراسب المتكون منه بالبريدين ويضاف له البنزوايل كلورايد وحامض الخليك المخفف ٨٠% للحصول على الدايل الذي يقطع بالصوديوم ابودايد للحصول عليه بالشكل الالديهايدي وهذا بدوره يفاعل مع مشتق الفوليك للحصول على ليكاند مشتق جديد وتم تشخيص الليكاندات بوساطة التحليل الدقيق للعناصر واطياف الاشعة تحت الحمراء والاشعة فوق البنفسجية وطيف الكتلة ودرجة الانصهار وقياس كروماتوكرافيا الطبقة الرقيقة كما تضمن البحث تحضير سلسلة جديدة من المعقدات من خلال مفاعلة الليكاندات اعلاه مع بعض املاح العناصر مثل :- النحاس (II) والنيكل (II) والكوبلت (II) والكادميوم (II) وشخصت المعقدات اعلاه بوساطة التحليل الدقيق للعناصر والرنين النووي المغناطيسي والكربون ١٣ والامتصاص الذري واطياف الاشعة تحت الحمراء والاشعة فوق البنفسجية والمرئية وقياس التوصيلية الكهربائية اضافة الى دراسة الحساسية المغناطيسية للمركبات وطيف الكتلة ودرجة الانصهار مع الفعالية البايولوجية وقياس كروماتوكرافيا الطبقة الرقيقة وبينت اطياف الاشعة تحت الحمراء فقدانا للمجموعة الامينية والاستعاضة عنها بالاصرة المزدوجة بين النتروجين والكربون دليلا على حدوث تفاعل قاعدة شف عند تناسق مشتق الفوليك مع ليكاندات محتوية على مجموعة كاربونيلىة قابلة للتفاعل مع المجموعة الامينية لمشتق الفوليك. كما بينت اطياف الاشعة تحت الحمراء سلوك الليكاند عند تناسقه مع بعض العناصر الفلزية وهذا السلوك يعود تفسيره الى التناسق مع الليكاندات المعوضة بمجاميع فعالة متنوعة وكما ياتي :- عند تناسق الليكاند مع كل من الكوبلت والنيكل والنحاس والكادميوم فانه يعطي مركبات مشحونة بشحنتين سالبتين ولقد استعملت اطياف الاشعة فوق البنفسجية وقياسات الحساسية المغناطيسية للمعقدات لدراسة التوزيع الفضائي لليكاندات مع ايونات الفلزات والاستدلال على الشكل الفضائي لها من خلال ما تقدم فان الشكل الفضائي المتوقع لمعقدات الكوبلت (II) والنيكل (II) والكادميوم (II) والنحاس (II) هي رباعية السطوح (هرم رباعي السطوح)

**الكلمات المفتاحية:** فيتامين بي، المنطقة الحمراء لمعقدات الكادميوم ، قواعد شف ، تقنية الطبقة الرقيقة ، النين النووي المغناطيس للبروتون واحد والكربون ١٣