New Schiff Base Derived From Folic Acid and 3-Aminoacetophenone and its Metal Complexes with Some Transition Metals and Evaluation of Their Biological Activity

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Abstract

The ligand [Potassium (E)-(4-(((2-((1-(3-aminophenyl) ethylidene) amino)-4-oxo-1,4-dihydropteridin-6-yl) methyl) amino)benzoyl)-L-glutamate] was prepared from the condensation reaction of folic acid with (3-aminoacetophenone) through Schiff reaction to give a new Schiff base ligand [H_2L]. The ligand [H_2L] was characterized by elemental analysis CHN, atomic absorption (A.A), (FT-I.R.), (U.V.-Vis), TLC, E.S. mass (for spectroscopes), molar conductance, and melting point. The new Schiff base ligand [H_2L], reacts with $Mn^{(II)}$, $Co^{(II)}$, $Ni^{(II)}$, $Cu^{(II)}$, $Cr^{(III)}$ and $Cd^{(II)}$ metal ions and (2-aminophenol), (metal : derivative ligand : 2-aminophenol) to give a series of new mixed complexes in the general formula:- $K_3[M_2(HL)(HA)_2]$, (where M=$Mn^{(II)}$ and $Cd^{(II)}$); $K_3[M_2(HL)(HA)_2.H_2O]$, (where M= $Cu^{(II)}$, $Ni^{(II)}$ and $Co^{(II)}$; and $K[Cr_2(HL)(HA)_2(H_2O)_3]$. 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, biological activity, TLC and magnetic moment measurements. From the above data the proposed molecular structure for $Mn^{(II)}$, $Co^{(II)}$, $Ni^{(II)}$, $Cu^{(II)}$, $Cr^{(III)}$ and $Cd^{(II)}$ complexes adopt a tetrahedral structure about the metal ions.

Key words: vitamin B_9, $Cd^{(+2)}$complexes infrared spectra , Schiff base, ^1H,^{13}C-NMR, TLC measurements.

Introduction

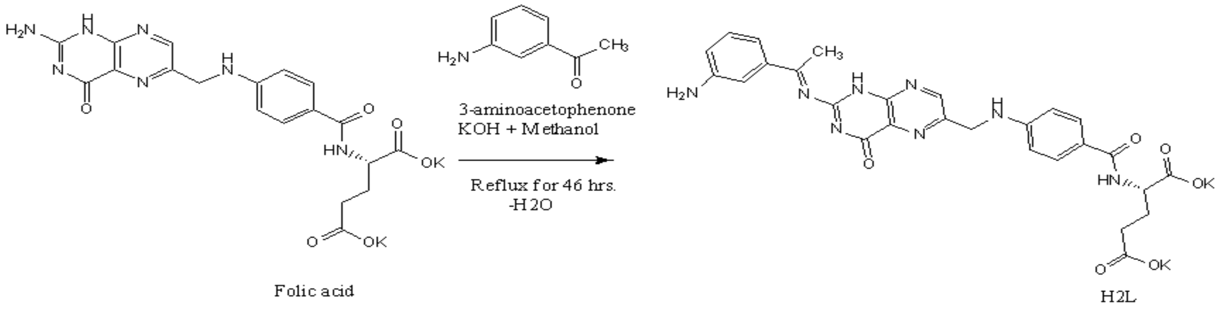
Folic acid (pteroylglutamic acid) heterocyclic compound is composed of three large sub-components. These are the pteridine ring, *para*-amino benzoic acid and glutamic acid, Fig.(1). Glutamic acid is an amino acid that the body can actually synthesize by itself and is found in proteins,[1] The folates are a group of heterocyclic compounds. They were the subject of previous recommendations prepared by the IUPAC-IUB commission on biochemical Nomenclature (CBN).[2] folic acid also known as vitamin M, vitamin B_9 [3], and vitamin B_c[4] (or folacin).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 an amine, or Schiff base. A Schiff base, named after Hugo Schiff, is a compound with a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group.[5] Schiff bases in a broad sense have the general formula $R_1R_2C=NR_3$, where R is an organic side chain. In this definition, Schiff base is synonymous with azomethine. Some restrict the term to the secondary aldimines (azomethines where the carbon is connected to a hydrogen atom), thus with the general formula RCH=NR.[6] Our study includes the synthesIs characterization and biological study of folic acid with mixed ligand (3-aminoacetophenone) and (2-aminophenole) through Schiff base reactions and their complexes with ($Mn^{(II)}$, $Co^{(II)}$, $Ni^{(II)}$, $Cu^{(II)}$, $Cr^{(III)}$ and $Cd^{(II)}$) transition elements.

Experimental

Reagents were purchased from Fluka and Redial – Dehenge Chemical Co. FT-I.R spectra were recorded as THERMO SCIENTIFIC, ID5, ATR NICOLET, IS5 FTIR spectrophotometer in the range (4000-400) cm^{-1}. Electronic spectra of the prepared compounds were measured in the region (200-900) nm for 10^{-3} M solutions in (DMSO) and distilled water 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.While metal contents 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^{-3} M solutions of the samples in (DMSO) and distilled water 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 are made in Department of Chemistry, Manchester University, U.K.

Synthesis of Schiff base ligand [H_2L]

[Potassium (E)-(4-(((2-((1-(3-aminophenyl)ethylidene)amino)-4-oxo-1,4-dihydropteridin-6-yl)methyl) amino)benzoyl)-L-glutamate]:- A solution of folic acid (2 g),(3.61 mmole) in methanol (20 ml)] was added to a mixture of little amount of KOH dissolved in small amount of hot distilled water (1 ml), and a solution of (3-aminoacetophenone) (0.488 g),(3.6 mmole) dissolved in (5 ml) methanol was added to the above mixture. And allow refluxing for (48 hrs.), then stirred at room temperature for (1 hr.). Mustard solid was collected by filtration. Scheme (1) and dried under vacuum for (24 hrs.), to give [H_2L] derivative ligand as a mustered solid, yield (1.5 g),(75 % yield), m.p (117-119 ^{0}C).



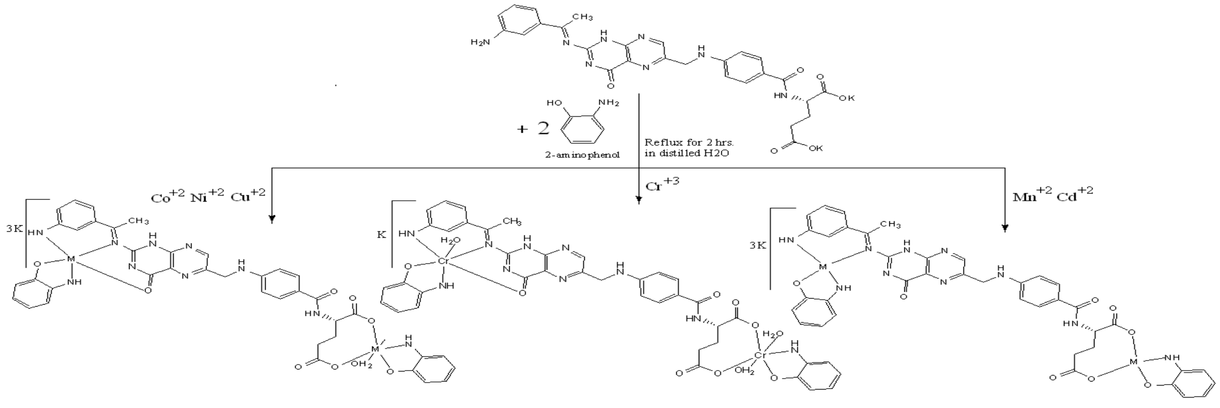
Scheme (1)

Synthesis of $K_3[Mn_2(HL)(HA)_2]$ complex

A solution of the derivative ligand [H_2L] (0.3g),(0.446 mmole) in a hot distilled water (20 ml), mixed with another solution of (2-aminophenol was[H_2A]) (0.097 g),(9.7 mmole) in a hot distilled water (5 ml), added slowly to a stirred solution of ($MnCl_2.4H_2O$),(0.176 g),(0.89 mmole) in (10 ml) distilled water. The resulting mixture was heated under reflux for (2 hrs.), 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 ^{0}C).

Synthesis of $K_3[Co_2(HL)(HA)_2.H_2O]$, $K_3[Ni_2(HL)(HA)_2.H_2O]$, $K_3[Cu_2(HL)(HA)_2.H_2O]$, $K[Cr_2(HL)(HA)_2(H_2O)_3]$ and $K_3[Cd_2(HL)(HA)_2]$ complexes

A similar method to that mentioned for preparing Mn^{II} complex was used to prepare the complexes of Schiff base ligand [H_2L] and (2-aminophenol [H_2A]) with (Co^{II}, Ni^{II}, Cu^{II} Cr^{III} and Cd^{II}) complexes. Scheme (2)., and Table (1) stated the quantities, reaction conditions and some physical properties of the prepared complexes



Scheme (2)

Results and Discussion

FT-I.R Spectral data for Schiff base ligand [H_2L]

The essential infrared data are summarized in Table (2).The F.T-IR. Spectra of the starting materials, folic acid and 3-aminoacetophenone are shown in Figs.(2) and (3). The two bands at (3414 and 3547 cm^{-1}) of folic acid, and (3369.6 and 3469.9 cm^{-1}) of 3-aminoacetophenone are due to the υ_{sy} (N-H) and υ_{asy} (N-H), respectively of the primary imines ($R\text{-}NH_2$) groups [7]. These bands are shifted to higher and lower frequency at (3367.7 and 3701 cm^{-1}) indicating forming of new derivative ligand [H_2L]. Fig.(5). Accompanied by the appearance of a new band at (1589 cm^{-1}) range assigned to the υ(C=N) stretching indicates Schiff base reaction [8,9]. The sharp absorption bands at (1668 cm^{-1}) and (1695 cm^{-1}), are due to the υ(C=O) stretching vibration of free keton group of 3-aminoacetophenone and folic acid, respectively,[10,11] . On the other hand folic acid exhibits three bands at (1606.7 cm^{-1}),(1485cm^{-1}) and (1413.8 cm^{-1}) assigned to the symmetric and asymmetric stretching vibration modes of (υ_{asy} COO^-), (υ_{asy} COO^-) and (COO^-) of carboxylic groups.[12] These peaks are still presented at (1575 cm^{-1}), (1508cm^{-1}) and (1400 cm^{-1}) range in the spectrum of the derivative ligand [H_2L] Fig(5). Compared with Folic acid as starting material. With {$\upsilon\Delta$=189 = (υ_{asy} COO^-) - (υ_{asy} COO^-)}.

The (U.V-Vis) spectrum of the Schiff base ligand [H_2L]

The (U.V-Vis) spectrum for [H_2L], Fig (12), exhibits a high intense absorption peak at (220 nm) (45454 cm^{-1}) ($\in_{max}$= 460 $molar^{-1}.cm^{-1}$), assigned for ($\pi\rightarrow\pi^*$). Shoulder peaks at (280 nm) (35714 cm^{-1}) ($\in_{max}$= 370 $molar^{-1}.cm^{-1}$) and (345 nm) (28985 cm^{-1}) ($\in_{max}$= 110 $molar^{-1}.cm^{-1}$) were assigned to ($n\rightarrow\pi^*$) transitions,[13,14] Table (3).

Synthesis of the complexes

The reaction of Schiff base ligand [H_2L] with (2-aminophnole [H_2A]) and (Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, Cr^{III}, 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 for all the complexes of (Mn^{II} , Co^{II}, Ni^{II}, Cu^{II} , Cr^{III}, and Cd^{II}) ion metals. The I.R. spectra, the essential infrared data are summarized in Table (2). The spectra of the derivative ligand [H_2L], Fig.(5) and (2-aminophenone[H_2A]) Fig.(4) shows two bands at (3367.7 and 3701 cm^{-1}) and (3305 and 3475 cm^{-1}) rang respectively, assigned to the stretching vibration of υ_s(N-H) and υ_{asy}(N-H) of amine group (NH_2),[7] are disappeared in the spectra of Mn^{II}, Ni^{II}, Co^{II}, Cu^{II}, Cr^{III} and Cd^{+2} complexes Figs.(6, 7, 8, 9, 10 and 11), and a new bands are formed at (3462 - 3306 cm^{-1}) range due to the stretching vibration of□□ υ(N-H) secondary amine ($R_2\text{-}NH$), because of reduced band order indicating the coordination with the metal ions through N and O atoms, and forming ring system. The band at (1589 cm^{-1}) range due to the υ(C=N) stretching [8,9] of the Schiff base ligand [H_2L], is shifted to lower and higher frequency at (1593 - 1573) rang for the complexes of Mn^{II}, Ni^{II}, Co^{II}, Cu^{II}, Cr^{III} and Cd^{II} as a result of forming ring system with the metal ions and delocalization of electron **π** density. The spectrum of the ligand [H_2L] exhibits two bands at (1508-1589 cm^{-1}) range due to υ_{asy}(COO^-), and one at (1400 cm^{-1}) range assigned to υ_{sy}(COO^-)[12]. And the {$\upsilon\Delta$= (υ_{asy} COO^-) - (υ_{asy} COO^-)}, {$\upsilon\Delta$=1589 -1400=189}. These three bands are shifted to lower and higher frequencies for all the complexes, indicating the forming of new compounds. The asymmetric and symmetric stretching vibration modes (υ_{sy}(COO^-) and υ_{asy}(COO^-)) of the COO^- group should help in elucidating the structure of the derivative ligands and their complexes. The direction of the frequency shift of the υ_{asy}(COO^-) and the υ_{sy}(COO^-) band with respect to those of the free ion depends on the coordination mode of the (COO^-) group with the metal ion. Nakamoto and McCarthy, claimed that if the coordination is monodentate, the υ_{asy}(COO^-) and the υ_{sy}(COO^-) will be shifted to higher and lower frequencies, respectively. Therefore all the $\upsilon_{asy}(COO^-)$ and the $\upsilon_{sy}(COO^-)$ groups of Mn^{II}, Ni^{II}, Co^{II}, Cu^{II}, Cr^{III} and Cd^{II} complexes are monodentate because they are shifted to different directions . [15,16] And the value of the $\upsilon\Delta=(\upsilon_{asy}COO^-) - (\upsilon_{asy}COO^-)\}$ for the complexes compared with the Schiff base ligand [H_2L] are :- ($\upsilon\Delta$, Mn= 254; $\upsilon\Delta$, Co= 248; $\upsilon\Delta$, Ni= 254; $\upsilon\Delta$, Cu= 195; $\upsilon\Delta$, Cr = 254; and $\upsilon\Delta$, Cd= 193.The observed broad bands at (3051-3258.9 cm^{-1}) rang are due to the υ (O-H) stretching of lattice water molecules, [17,18] of the Co^{II}, Ni^{II}, Cu^{II}, and Cr^{III} (bar Mn^{II} and Cd^{II} complexes, metal oxygen and metal nitrogen band further confirmed by the presence of peaks at (520-586 cm^{-1}) and (420-470 cm^{-1}) range were assigned to υ(M-O) [19], and υ(M-N) , [20] stretches for the Mn^{II}, Ni^{II}, Co^{II}, Cu^{II}, Cr^{III} and Cd^{II} complexes, respectively.

The (U.V-Vis.)

The (U.V- Vis) Spectra of the Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, Cr^{III} and Cd^{II} complexes, respectively. Table (3) summarized the absorption peaks of the complexes. The (U.V) spectra of Mn^{II} and Cd^{II} complexes Figs.(13) and (18) respectively showed two intense peaks in the range (256 nm), (39062 cm^{-1}), ($\in_{max}$ =419 $molar^{-1}$. cm^{-1}) and (259 nm), (39370 cm^{-1}), ($\in_{max}$ =500 $molar^{-1}$. cm^{-1}) range assigned to the ligand field for Mn^{II} and Cd^{II}, respectively[21]. Another two peaks at (418 nm), (23923 cm^{-1}), ($\in_{max}$ =290 $molar^{-1}$. cm^{-1}) and (418 nm),(23923 cm^{-1}), ($\in_{max}$ =663 $molar^{-1}$. cm^{-1}) range assigned to the charge transfer transition for Mn^{II} and Cd^{II} respectively[22]. The third peak detected in the visible region for Mn^{II} complex at (436 nm),(22935 cm^{-1}),($\in_{max}$ =936 $molar^{-1}$. cm^{-1}) is due to $({}^6A_1 \rightarrow {}^4A_{1(G)})$ transition, indicating a tetrahedral structure[22] around Mn^{II}. The third peak for Cd^{II} complex at (436 nm),(22935 cm^{-1}),($\in_{max}$ =688 $molar^{-1}$. cm^{-1}) is assigned to charge transfer transition[23], suggesting a tetrahedral structure around Cd^{II} ion. Since the metal ion of compounds belongs to (d^{10}) system, this peak is assigned to charge transfer transitions and this is in according compound with results reported by Ramesh and coworkers [24]. In the case of the spectra of (2), (3) and (4) Figs.(14), (15) and (16), respectively the intense peaks in the (U.V) region at (224-274) and (294 418) rang for Co^{II}, Ni^{II} and Cu^{II} assigned to ligand field and charge transfer transitions about respectively. [21] Peaks at (436 nm) (22935 cm^{-1}) ($\in_{max}$ =936 $molar^{-1}$. cm^{-1}), (416 nm) (24038 cm^{-1}), ($\in_{max}$ =269 $molar^{-1}$. cm^{-1}) and (414 nm) (24154 cm^{-1}) ($\in_{max}$ =275 $molar^{-1}$. cm^{-1}) range of (2), (3) and (4) complexes, respectively were assigned to $({}^4A_{2(F)} \rightarrow {}^4E_{(p)})$, $({}^1A_1 \rightarrow {}^1E)$ and $(e' \rightarrow a_1)$ [22]. (d-d) transitions suggesting a trigonal-bipyramidal structures around (Co^{II} and Cu^{II}) ions, and square pyramidal structure around Ni^{II}.[22] The (U.V) spectrum of complex (5) Fig.(17) showed two intense peaks in the range (260 nm),(38461 cm^{-1}), ($\in_{max}$ =907 $molar^{-1}$. cm^{-1}) and (291 nm) (34364 cm^{-1}), ($\in_{max}$ =1126 $molar^{-1}$. cm^{-1}) assigned to ligand field and charge transfer transition[21]. The strong peak at the visible region at (353 nm), (28328 cm^{-1}), ($\in_{max}$= 303 $molar^{-1}$. cm^{-1}) is assigned to $({}^4A_2g \rightarrow {}^4T_2g_{(p)})$ transition, confirming a trans octahedral structure around Cr^{III} ion complex[22].

The molar conductance

The molar conductance of the complexes in (DMSO) lies in the (81-87 $ohm^{-1}.cm^2.mole^{-1}$) range indicating the complexes are electrolyte with 1:3[25]. Bar Cr^{III} complex where it lie in the (30 $ohm^{-1}.cm^2.mole^{-1}$) range indicating the complex is electrolyte with 1:1[26]. The electronic spectral data of the complexes are summarised in (Table-3).

The magnetic moment

The magnetic moment values for the of $K_3[Co_2(HL)(HA)_2.H_2O]$ complex indicated trigonalbi-pyramidal geometry around Co^{II} metal ion. According to the calculated and expected values of the μ_{eff} which is lies in (3.93 B.M.) of the complexes indicating paramagnetic [27].

^{1}H-NMR Spectrum

^{1}H-NMR Spectrum of $K_3[Cd_2(HL)(HA)_2]$ complex:-The ^{1}H-NMR spectrum for $K_3[Cd_2(HL)(HA)_2]$ complex in DMSO-d^6 Fig.(19) showed single signal peak appear at (δ 1.31 ppm-CH)(3H) attributed to methyl groups. The quartarete signal obtained at (δ 2.4 ppm-CH)(4H) due to methylene CH_2 group. The triplet signal obtained at (δ 3.0 ppm-CH)(3H) due to methylene CH_2 group has shifted to low field as a result of the effect of C=O group. A single signal obtained at (δ 4.0 ppm-NH)(1H) assigned to (C-NH) aromatic. A signal at (δ 4.90 ppm-CH)(1H) due to methylene CH_2 group has shifted to low field because of the cycle effect from one side and N-H group effect of the other side. The triplet signal at (δ 5.20 ppm-CH)(3H) due to methane (CH_2) group. This group has shifted to low field as a result of the effect of (NH sec.) amide group and C=O. Four signals are due to benzylidenimine, doublet signal at (δ 6.51 ppm-CH)(2H), single signal at(δ 7.42 ppm-CH)(1H), triplet signal at (δ 7.60 ppm-CH)(3H) and doublet signal at(δ 7.80 ppm-CH)(2H). A single signal at (δ 8.5 ppm-CH)(1H) is due to (-CH=N) 2-pyrazine group. A signal at (δ 9.02 ppm)(1H) is due to (NH) amide group. And multiple group of resonance signals at (δ 6.20-7.90 ppm-CH) range is due to benzene ring. The NMR spectral data of $K_2[Cd_2(L)HA_2]$ complex was compared with the spectral data for the ligand according to chemoffes program. Table (4) summarized the details of the chemical shifts.

^{13}C-NMR Spectrum of $K_3[Cd_2(HL)(HA)_2]$ complex

The ^{13}C-NMR spectrum of the $K_3[Cd_2(HL)(HA)_2]$complex in DMSO-d6 solvent shown in Fig.(20). The characterization of chemical resonances are listed in Table (5).

E.S-mass Spectrum of the derivative ligand [H_2L]

The E.S-mass (+) spectrum of Schiff base ligand [H_2L], Fig.(21) shows the parent ion peak at (M/Z=634.11), which corresponds to $(M)^+$. Peak detected at [M/Z=657.0 is assigned for $(M+Na)^+$, other fragments are summarized in Table (6).

Biological activity for the Schiff base ligand [H_2L]

The biological activity of the Schiff base ligand (H_2L) is studied by using inhibition method. [28-31] for four types of pathogenic bacteria. Two types of bacteria were gram positive which are *staphylococcus aureu*and *bacillus subtilis*, the second two were gram negative which are *escherichiacoli* and *psedomonasaeruginosa*. The Schiff base ligand (H_2L) did not show any inhibition diameter against any type of the four bacterial, neither after 24 hrs. nor after 48 hrs., as shown in Table (7). But the results indicate that there complexes show more activity than the ligands under similar experimental conditions with the same kinds of bacteria.

Thin-layer chromatography (TLC) measurement

The T.L.C technique measurement for the Schiff base ligand (H_2L] was performed with Mn^{+2}, Co^{+2}, Ni^{+2}, (Cu^{+2}, Cr^{+3}, and Cd^{+2} complexes and resulting the appearance of a new spots in different positions belong to (Mn^{+2}), Co^{+2}, Ni^{+2}, Cu^{+2}, Cr^{+3}, and Cd^{+2} ion complexes these spots position are differ from the position of the starting materials spots about (3.2 mm) range indicating the forming of a new compounds. As in the T.L.C chromatography for $K_3[Ni_2(HL)(HA)_2.H_2O]$ complex.

The proposed molecular structure

The proposed molecular structure of $K_3[Ni_2(HL)(HA)_2.H_2O]$ complex according to chem. office program display band angles and band lengths, table (8) and the proposed geometrical shape of the complex is trigonalbipyramedal Fig.(22)

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Table (1): some physical properties of the Schiff base ligand [H_2L] and its complexes.

Empirical formula	M.W	Yield %	w.t of metal Ion= mmole	w.t of product=g	m.p° C	Color	Found, (Cal.) %				
							C	H	N	K	Metal
[H_2L]	634.73	75	-	1.5	117-119	Mustard	(51.09)47.25	(3.81) 3.00	(17.65)15.28	(12.32) 10.00	-
$K_3[Mn_2(HL)(HA)_2]$	996.91	76.6	0.89	0.23	240 (dec.)	Deep-Brown	(46.99)54.11	(3.43) 2.66	(14.05)12.22	(11.77) 10.00	(11.02) 9.12
$K_3[Co_2(HL)(HA)_2.H_2O]$	1058.95	70	0.942	0.20	249 (dec.)	Brown	(44.23)43.45	(3.71) 2.66	(13.23)12.18	(11.08) 9.20	(11.13) 10.18
$K_3[Ni_2(HL)(HA)_2.H_2O]$	1058.47	80	0.943	0.22	220 (dec.)	Green	(44.25)43.80	(3.71) 2.50	(13.23)11.01	(11.08) 9.98	(11.09) 10.01
$K_3[Cu_2(HL)(HA)_2.H_2O]$	1068.17	73	0.939	0.23	248 (dec.)	Deep-Brown	(43.85)42.09	(3.68) 2.10	(13.11)12.00	(10.98) 9.61	(11.90) 9.00
$K[Cr_2(HL)(HA)_2(H_2O)_3]$	963.23	63	0.943	0.19	232 (dec.)	Deep-Brown	(48.48)46.12	(4.07) 3.10	(14.49)13.50	(4.04) 3.61	(10.76) 9.49
$K_3[Cd_2(HL)(HA)_2]$	1111.86	63	0.944	0.25	230 (dec.)	Pal-Brown	(42.13)41.41	(2.99) 2.00	(12.00)11.11	(10.55) 9.76	(20.22) 19.11

(Calcu.): calculated (dec.): decom

Table (2): FT-I.R. spectral data (wave number υ) cm^{-1} of the Schiff base ligand (H_2L] and its complexes

Compound	υ(N-H) Primary $R-NH_2$	υ(N-H) Secondary R_2-NH	υ(O-H) H_2O	υ(C=O)	υ(COO^-)as υ(COO^-)s	υ(C=N) imin.	υ(CH_3)	υ(C-N)aroma υ(C-N)aliph.	M- O M- N
$K_2[C_{27}H_{24}N_8O_6]$ $[H_2L]$	3701(br.) 3367.7(br)	- -	-	1610(w.)	1575(m) 1508(sh) 1400(sh)	1589(s)	1334(sh)	1292(br) 1174.6(s)	- -
2-aminophenole $[H_2A]$	3475(sh) 3305(sh)	-	3051(br)	-	- -	-	-	- 1217	- -
$K_3[Mn_2(HL)(HA)_2]$	- -	3412(w)	-	1573(w)	1654.9(w.) 1573.9(br.) 1400(br.)	1589(br.)	1325(sh)	1338.6(w) 1203(sh)	584(sh) 470(sh)
$K_3[Co_2(HL)(HA)_2.H_2O]$	- -	3369.6(w)	3151.6(br.)	-	1654.9(w.) 1546.9(br.) 1406(w)	1585(w)	1330(sh)	1342(br.) 1273(w)	584(sh) 470(sh)
$K_3[Ni_2(HL)(HA)_2.H_2O]$	- -	3317.8(sh) -	3258.9(sh)	-	1650(w) 1448.6(br) 13 96(w)	1593(w)	1300(sh)	1373(br) 1280.7(br.)	520(sh) 420(sh)
$K_3[Cu_2(HL)(HA)_2.H_2O]$	- -	3462(w) -	3253.9(br)	-	1595(w) 1508(w) 1400(w)	1573(br)	1340(sh)	1350(br) 1294(br)	586(sh) 450(sh)
$K[Cr_2(HL)(HA)_2(H_2O)_3]$	- -	3412(sh)	3248(br)	-	1654.9(w) 1585(w) 1400(w)	1573.9(s)	1300(sh)	1357(w) 1273(br.)	584(sh) 420(sh)
$K_3[Cd_2(HL)(HA)_2]$	- -	3375(sh) 3306(sh)	-	1595	1595(w) 1512(w) 1402(w)	1573(w)	1325(sh)	1344(br.) 1267(sh)	584(sh) 465(sh)

strong vs: very strong m: medium w: weak s,sh: strong sharp br: broad
o.o.p: out of plane aliph: aliphatic arom: aromatic υ: stretching δ: bending

Table (3): Electronic spectral data of derivative ligand (H_2L] and it's metal complexes

Compound	λ nm	υ cm^{-1}	∈max $molar^{-1}$. Cm^{-1}	Assignment	Geometrical shape	Solvent	Ratio	M.C*(ohm^{1}.cm^{2}.$mole^{-1}$)
[H_2L]	220	45454	460	$\pi \rightarrow \pi^*$	-	-	-	-
	280	35714	370	$n \rightarrow \pi^*$				
	345	28985	110	$n \rightarrow \pi^*$				
$K_3[Mn_2(HL)(HA)_2]$	256	39062	419	Ligand field	Tetrahedral	DMSO	1:3	85
	418	23923	290	*Ch.T*				
	436	22935	303	$^6A_1 \rightarrow {}^4A_{1(G)}$				
	510	19607	60	$^6A_1 \rightarrow {}^4A_{1(G)}, {}^4E$				
$K_3[Co_2(HL)(HA)_2.H_2O]$	224	36630	900	*Ligand field*	Trigonalbi-pyramidal	DMSO	1:3	85
	418	23923	908	Ch.T				
	436	22935	936	$^4A'_{2(F)} \rightarrow {}^4A'_{2(P)}$				
	500	20000	300	$^4A'_{2(F)} \rightarrow {}^4E''_{(p)}$				
$K_3[Ni_2(HL)(HA)_2.H_2O]$	259	38610	1158	*Ligand field*	Square pyramidal	DMSO	1:3	86
	294	34013	1003	*Ch.T*				
	416	24038	269	$^1A_1 \rightarrow {}^1E'$				
	440	22727	190	$^1A_1 \rightarrow {}^1E''$				
$K_3[Cu_2(HL)(HA)_2.H_2O]$	274	36496	360	Ligand field	Trigonabi-Pyramidal	DMSO	1:3	87
	334	29940	232	*Ch.T*				
	414	24154	275	$e' \rightarrow a_1$				

	510	**19607**	**150**	$e'' \rightarrow a_1$				
$K[Cr_2(HL)(HA)_2(H_2O)_3]$	**260**	**38461**	**907**	***Ligand field***	**Octahedral**	**DMSO**	**1:1**	**30**
	291	**34364**	**1126**	***Ch.T***				
	353	**28328**	**303**	${}^4A_2g \rightarrow {}^4T_1g_{(F}$				
	445	**22471**	**100**	${}^4A_2g \rightarrow {}^4T_2g$				
$K_3[Cd_2(HL)(HA)_2]$	**259**	**39370**	**500**	**Ligand field**	**Tetrahedral**	**DMSO**	**1:3**	**81**
	418	**23923**	**663**	***Ch.T***				

Table (4) :^{1}H-NMR Spectral data of $K_3[Cd_2(HL)(HA)_2]$

Group	**Funct. group**	δ (ppm)
Methane	$C_{(28)}$ –H	5.20
1-benzene	$C_{(2,3,4,5.......)}$-H	6.20-7.90
2-pyrazine	$C_{(19)}$-H	8.5
Benzylidenimin	$C_{(8,10,11,12)}$-H	6.51-7.80
Methylene	$C_{(21,31,32)}$-H_2	4.90, 3.0 , 2.4
Methyl	$C_{(14)}$-H_3	1.31
aromatic C_{15} -NH	$C_{(15)}$ -NH (s)	4.0
Amide	$C_{(28)}$-NH (s)	9.02
DMSO solvent		2.5

Table (5) $^{:13}$C-NMR Spectral data of $K_3[Cd_2(HL)(HA)_2]$

Group	C^{13}	δ (ppm)
Pyrazine	C (17,18,20)	133-152
Imine	C (13,15)	168-165
Carbonyl	C (16)	189
Benzen	C (…1,6,7,9,11)	134,145,147,148,123,131
Amide	C (28)	167
Carboxyl	C (29,33)	177
DMSOsolvent		30
Pyrazine	CH (19)	145
Benzen	CH (….4,3,2)	118,120,128,127,110,115,116,
Aliphatic	CH (30)	57
Aliphatic	CH_2 (21,31,32)	28,27,29
Aliphatic	CH_3 (14)	20

Table (6): E.S-mass Spectral data of derivative ligand $[H_2L]$.

Fragmentations	Mass/charge (m/z)	Relative abundance
$[M]^+$	634.11	22
$[M-\{C_2H_5\}]^+$	543.O7	9
$[M-\{C_2H_5-C_2H_3N\}]^+$	502.0	30
$[M-\{C_2H_5-C_2H_3N-C_5H_4O\}]^+$	370.3	35
$[M-\{C_2H_5-C_2H_3N-C_5H_4O-C_2H_5N\}]^+$	326.9	18
$[M-\{C_2H_5-C_2H_3N-C_5H_4O-C_2H_5N-CKO_2\}]^+$	245.05	35
$[M-\{C_2H_5-C_2H_3N-C_5H_4O-C_2H_5N-CKO_2-C_4H_4O_2\}]^+$	121.0	40
$[M-\{C_2H_5-C_2H_3N-C_5H_4O-C_2H_5N-CKO_2-C_4H_4O_2-CHNO\}]^+$	78.03	8

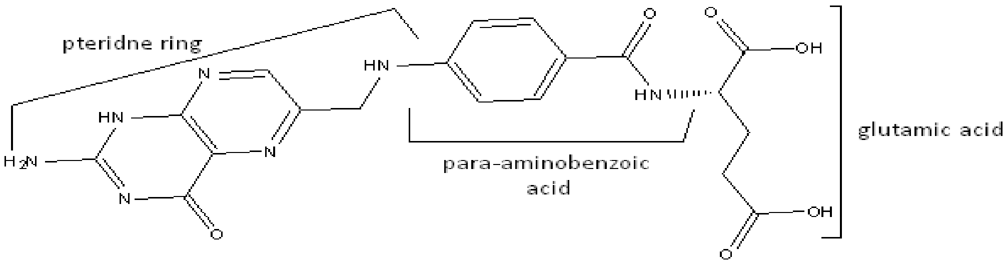
Table (7): Inhibition circle diameter in millimeter for the ligands after 24 hrs. , and after 48 hrs.

Compounds	Time	Staphylococcus aureu	Pseudomonas aeruginosa	Bacillus subtilis	Escherichia coli
$[H_2L]$	24 hrs.	–	–	–	–
$[H_2L]$	48 hrs.	–	–	–	–

Table (8): The proposed Bond Lengths and bond angles of $K_3[Ni_2(HL)(HA)_2.H_2O]$

Type of bond	Bond length (A˚)	Type of angles	Bond length (A˚)
Ni-O	1.790	O-Ni-O	90.000
Ni-N	1.826	O-Ni-N	180.000
N-H	1.050	Ni-O-C	124.455
C-H	1.100	H-N-Ni	125.500
C-N	1.356	N-Ni-O	90.000
C-C	1.397	N-Ni-N	90.000
C-O	1.208	H-N-C	125.500
		C-N-Ni	109.000
		Ni-N-C	152.746

(A˚)= Angstrom,, (˚)= degree



Fig(1) :the structure of folic acid

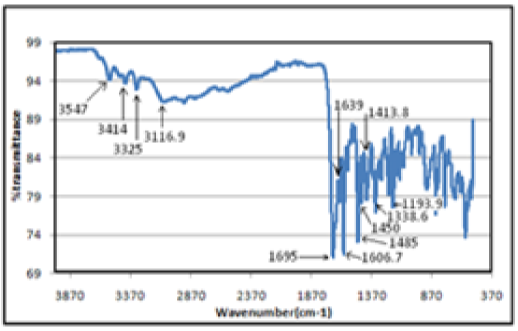


Figure (2) FT.IR spectrum folic acid

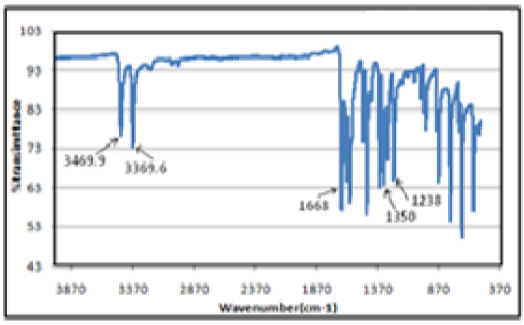


Figure (3) FT.IR spectrum of 3-aminoacetophenone

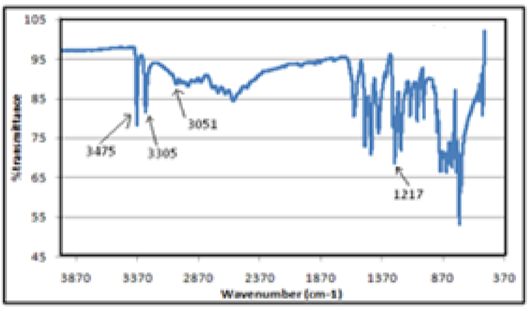


Figure (4) FT.IR spectrum of 2-aminoacetophenol

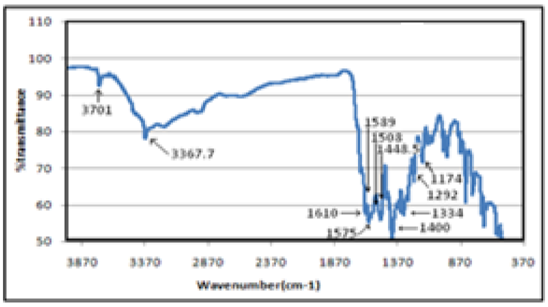


Figure (5) FT.IR spectrum of $[H_2L]$ ligand

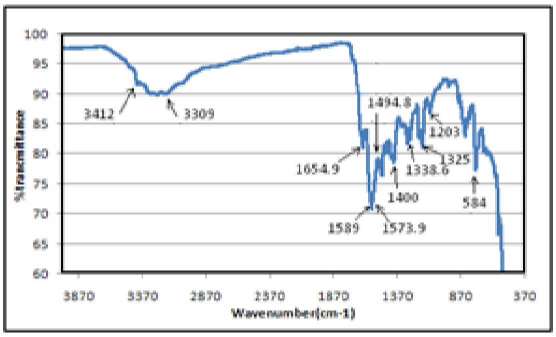


Figure (6) FT.IR spectrum of $K_3[Mn_2(HL)(HA)_2]$

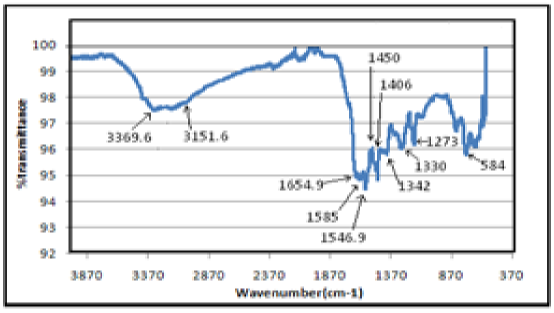


Figure (7) FT.IR spectrum $K_3[Co_2(HL)(HA)_2.H_2O]$

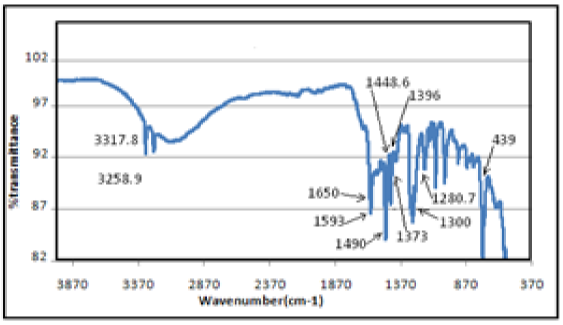


Figure (8) FT.IR spectrum of $K_3[Ni_2(HL)(HA)_2.H_2O]$

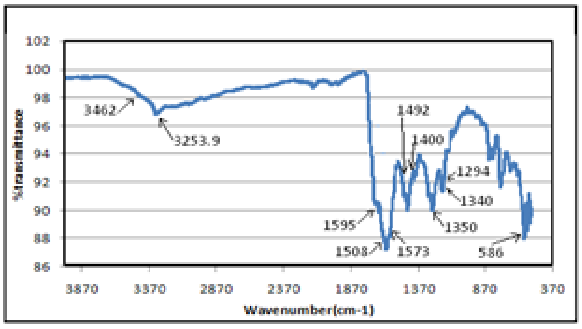


Figure (9) FT.IR spectrum of $K_3[Cu_2(HL)(HA)_2.H_2O]$

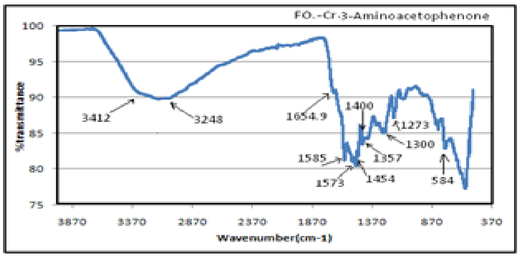


Figure (10) FT.IR spectrum of $K[Cr_2(HL)(HA)_2(H_2O)_3]$

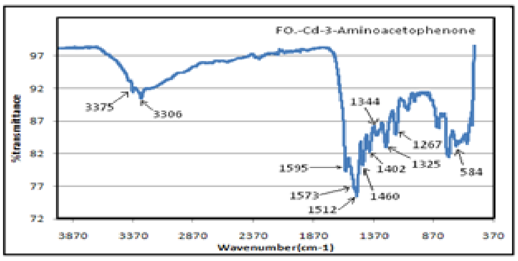


Figure (11) FT.IR spectrum of $K_3[Cd_2(HL)(HA)_2]$

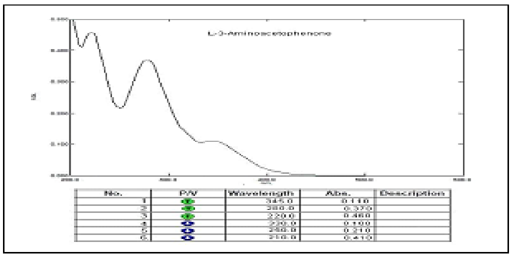


Figure (12) The U.V-Vis. spectrum of $[H_2L]$ ligand

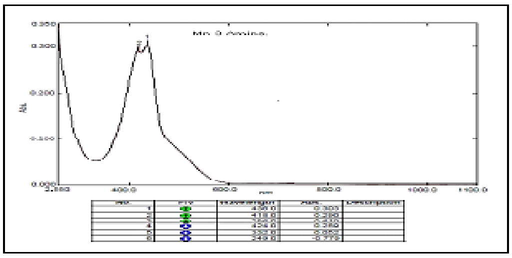


Figure (13) The U.V-Vis. spectrum of $K_3[Mn_2(HL)(HA)_2]$

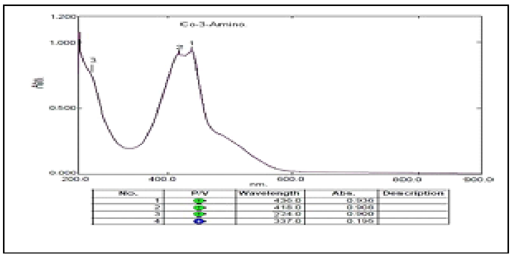


Figure (14) The U.V-Vis. spectrum of $K_3[Co_2(HL)(HA)_2.H_2O]$

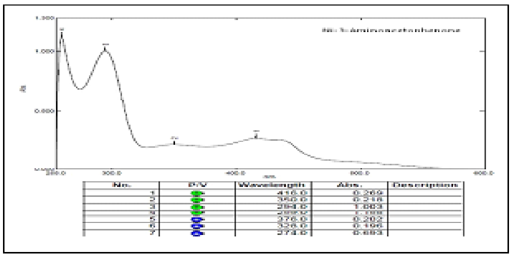


Figure (15) The U.V-Vis. spectrum of $K_3[Ni_2(HL)(HA)_2.H_2O]$

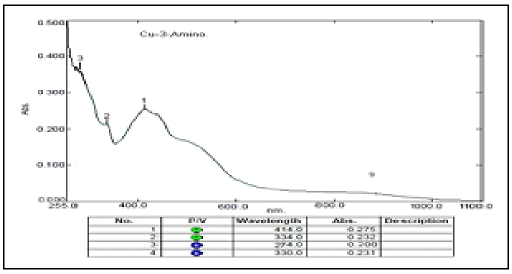


Figure (16) The U.V-Vis. spectrum of $K_3[Cu_2(HL)(HA)_2.H_2O]$

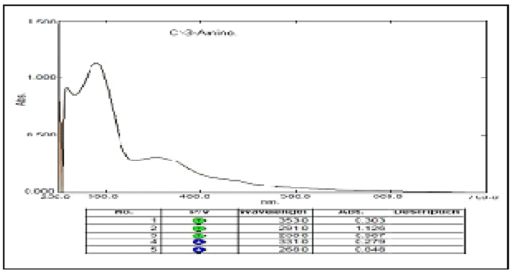


Figure (17) The U.V-Vis. spectrum of $K[Cr_2(HL)(HA)_2(H_2O)_3]$

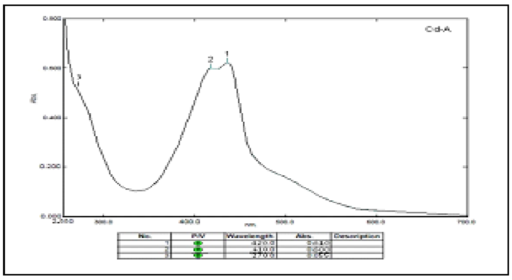
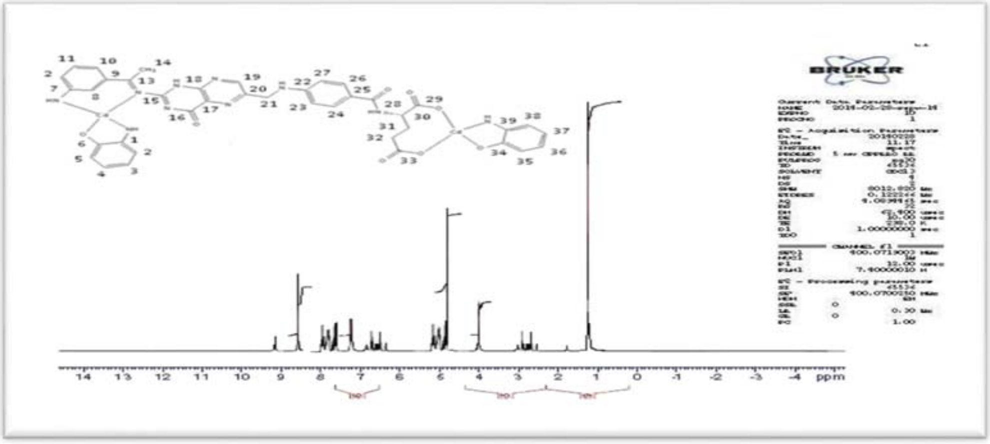
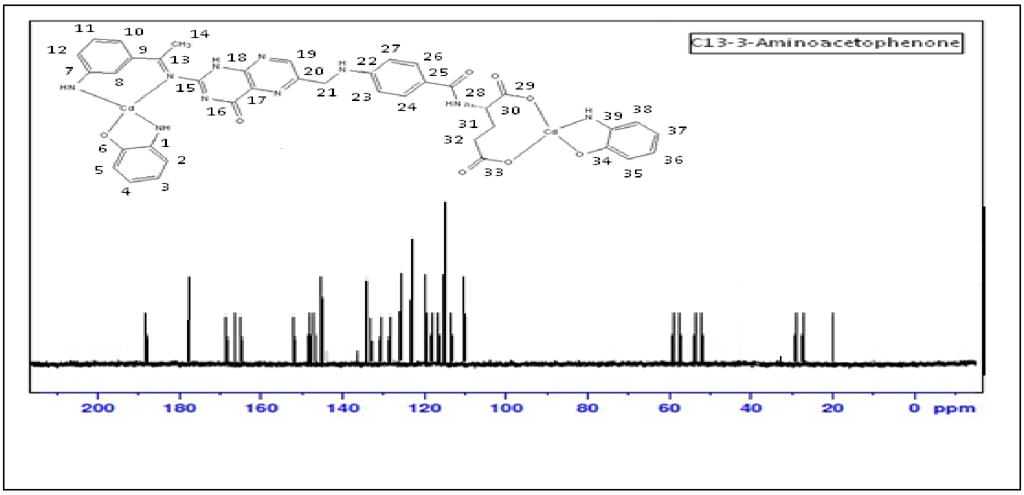


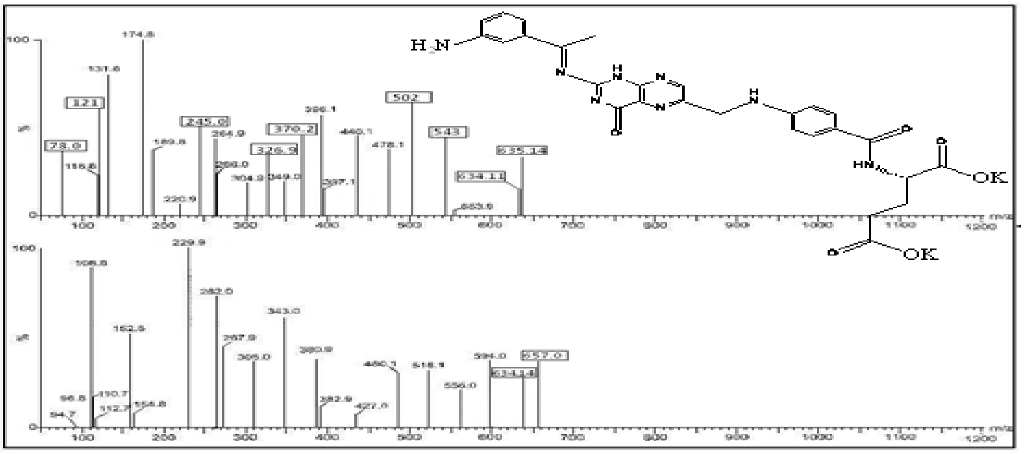
Figure (18) The U.V-Vis. spectrum of $K_3[Cd_2(HL)(HA)_2]$



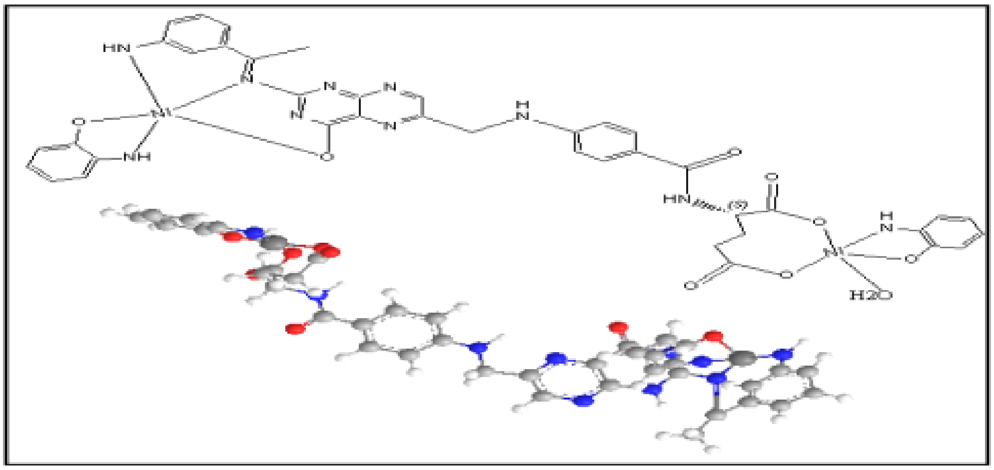
Fig(19): The ^{1}H-NMR spectrum for $K_3[Cd_2(HL)(HA)_2]$ complex in DMSO-d^6



Fig(20): The ^{13}C-NMR spectrum of the $K_3[Cd_2(HL)(HA)_2]$complex in DMSO-d6 solvent



Fig(21): The E.S-mass (+) spectrum of Schiff base ligand [H_2L],



Fig(22) : The proposed molecular structure of $K_3[Ni_2(HL)(HA)_2.H_2O]$ complex:

تحضير وتشخيص قاعدة شف جديدة مشتقة من حامض الفوليك و (3- امينو اسيتوفينون) ومعقداتها المختلطة مع بعض الفلزات الانتقالية ودراسة فاعليتها البايولوجية

احمد ثابت نعمان
خالد فهد علي
ايمان ابراهيم عبد الكريم
قسم الكيمياء/ كلية التربية للعلوم الصرفة(ابن الهيثم)/جامعة بغداد

استلم البحث في :15 تشرين الاول2014، قبل البحث في:2 شباط 2015

الخلاصة

تضمن البحث تحضير ليكند 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 ذات الصيغة:-

بالصيغة العامة:- $K[Cr_2(HL)(HA)_2(H_2O)_3]$

حيث M=Mn, Cd $K_3[M_2(HL)(HA)_2]$

حيث M=Co, Ni, Cd $K_3[M_2(HL)(HA)_2.H_2O]$

تم تشخيص الليكاند بوساطة التحليل الدقيق للعناصر واطياف الاشعة تحت الحمراء والاشعة فوق البنفسجية وطيف الكتلة والفعالية البايولوجية ودرجة الانصهار وقياس كروماتوكرافيا الطبقة الرقيقة كما تضمن البحث تحضير سلسلة جديدة من المعقدات من خلال مفاعلة الليكاند اعلاه مع بعض املاح العناصر مثل :- المنغنيز (II) والكوبلت (II) والنيكل (II) والنحاس (II) والكروم (III) والكادميوم (II) وشخصت المعقدات اعلاه بوساطة التحليل الدقيق للعناصر والرنين النووي المغناطيسي والكاربون 13 والامتصاص الذري واطياف الاشعة تحت الحمراء والاشعة فوق البنفسجية والمرئية وقياس التوصيلية الكهربائيةفضلا عن 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 النيتروجين والكاربون دليلا على حدوث تفاعل قاعدة شف عند تناسق مشتق الفوليك مع ليكاندات كيتونية محتوية على مجموعة كاربونيلية 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 وكما ياتي :- عند تناسق الليكند مع المنغنيز والكادميوم فانه يعطي مركبات متعادلة اما عند تناسقه مع النيكل والنحاس والكوبلت فانه يعطي مركبات مشحونة بشحنة سالب واحدة وعند تناسقه مع الكروم فانه يعطي مركبا مشحونا بشحة موجبة واحدة ولقد استعملت اطياف الاشعة فوق البنفسجية وقياسات الحساسية المغناطيسية للمعقدات لدراسة التوزيع الفضائي لليكاندات مع ايونات الفلزات والاستدلال على الشكل الفضائي لها. ومن خلال ما تقدم :-

1- فان الشكل الفضائي المتوقع لمعقدات المنغنيز(II) والكادميوم(II) هي رباعية السطوح

2- الشكل الفضائي المتوقع لمعقدات النيكل (II) والنحاس (II) والكوبلت (II) هوخماسي السطوح

3-الشكل الفضائي المتوقع لمعقد الكروم (III) هو ثماني السطوح

الكلمات المفتاحية : فيتامين بي ، المنطقة الحمراء لمعقدات الكادميوم ، قواعد شف ، تقنية الطبقة الرقيقة ، النين النووي المغناطيس للبروتون واحد والكاربون 13