Synthesis, Characterization and Biological Studies Of metal Complexes of *m* - Amino Benzoic Acid.

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Abstract

Reaction of bidentate *m*-amino benzoic acid (mABAH) with metal salts of (Cu(II), Pb(II), Zn(II), Mn(II), Co(II), Cd(II), Ni(II)) yields the new complexes of type $[M(mABA)_2]$ (where M = Cu(II), Pb(II) or Zn(II), Mn(II), Cd(II)), and $[Hg(mABA)(H_2O)Cl]$ and $[M(mABA)_2(H_2O)_2]$ (where M = Co(II), Ni(II)). The metal complexes were characterized by elemental analysis, molar conductance and IR spectra confirm coordination through nitrogen atom of amine group and the oxygen atom of the carboxylic anion group to the central metal ion. The magnetic moment data suggested for all complexes to have a tetrahedral and octahedral geometry around the central metal ion. The electronic spectral data also agree with their proposed structures. Biological activity of the ligands (mABAH) and their metal complexes were tested against gram positive bacteria (***Staphylococcus arreus***) and gram negative bacteria (***Escherichia coli.*** and ***Pseudomonas aeruginosa***).

Key words: - *m*-amino benzoic acid, metal salts, antibacterial activity.

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تحضير,تشخيص ودراسة الفعالية البايلوجية للمعقدات المعدنية ل (ميتا- امين حامض البنزويك)

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الخلاصة

ان تفاعل الليكاند ميتا- امين حامض البنزويك (mABAH) ثنائي السن مع الاملاح المعدنية ل (Cu(II), Pb(II), Zn(II), Mn(II), Co(II), Cd(II), Ni(II)) يعطي معقدات حديثة من النوع : $[M(mABA)_2]$ حيث (Cu(II),) و $[M(mABA)_2(H_2O)_2]$ حيث (M = Co(II), Ni(II)) و Pb(II) or Zn(II), Mn(II), Cd(II) = M) و $[Hg(mABA)(H_2O)Cl]$). تم تشخيص المعقدات المحضرة بواسطة التحليلِ الدقيق للعناصر، و قياس التوصيلية الكهربائية و اطياف الاشعة تحت الحمراء التي اكدت ارتباط الليكاند عن طريقذرة النيتروجين لمجموعة الامين و هيدروكسيل مجموعة الكاربونيل بالذرة المركزية. ونتائج الحساسية المغناطيسية اقترحت الهيئة الهندسية رباعي السطوح حول الذرة المركزية. ونتائج الاشعة فوق البنفسجية – المرئية ايضا اكدت الاشكال المقترحة . الفعالية البايولوجية لليكاند (mABAH) و معقداتها اختبرت مقابل ثلاثة اوساط بكتيرية هي (***Staphylococcus aureus*** و ***Pseudomonas aeruginosa*** و ***Escherichia coli***.).

الكلمات المفتاحية: ميتا - امين حامض البنزويك, املاح الفلزات , الفعالية البايولوجية.

Introduction

The application of coordination chemistry is more relevant in pharmaceutical preparations formulated to treat specific diseases associated with problems over the management of essential metals in vivo,[1]. Metal complexes are important in medicine one of the important uses of metal complex in therapy is to treat illness resulting from a deficiency of essential metals. As examples, iron dextran complexes are used to treat anemia due to iron deficiency and cobalt, in the form of vitamin (B_{12}), [2] is used to treat pernicious anemia resulting from vitamin (B_{12}) deficiency,[3,4].

The use of multifunctional ligands - whose donor atoms are on a rigid phenyl group - is very important for coordination with metals,[5]. In the series of amino benzoic acids, an important ligand is *m*-amino benzoic acid (mABAH) which has immense applications in biology,[6] . For this purpose, it is particularly interesting in employing aromatic amino acids such as (a, b, c), for two reasons: first, they contain carboxylate and amino functionalities, which are known to behave differently towards metal centers because of differences in their hard-soft donor characteristics. Second, by choosing the second substituent's position (namely, a-ortho, b-meta, and c-para; i.e. 60, 120 or 180° between the functional groups) one can easily vary the resultant compounds,[6].

Experimental

All chemicals were of highest purity and used as received.

Physical measurement and analysis:

Elemental analyses were recorded on OCI Spectroscopy (C.H.N.) analyzer and Perkin Elmer-2400 (C.H.N.S.) analyzer. The molar conductance measurement were recorded in DMSO (10^{-3} M) using conductivity meter model Conductometer type (Cond. 720) conductivity meter. Melting points were measured on a (Stuart Digital) melting point apparatus. The I.R. Spectra of the ligand and complexes were recorded on a Shimadza Infrared Spectrophotometer in the (200-4000) cm^{-1} rang using CsI discs and Perkin Elmer FT-IR-Spectrophotometer in the (400-4000) cm^{-1} rang using KBr discs. Magnetic measurement data were recorded on a Brucker BM6 instrument at room temperature following the Gouy method. Electronic spectra of the ligand and it's complexes were recorded in DMSO using a Jenway 6485 spectrophotometer.

Synthesis of Complexes :

The complexes was synthesized by mixing an ethanolic solution of (0.02) mole of *m*-amino benzoic acid with (0.01) mole of metal salts of ($CuCl_2$, $Pb(CH_3COO)_2$, $Zn(CH_3COO)_2$, $MnCl_2$, $CoCl_2$, $Cd(NO_3)_2.7H_2O$, $NiCl_2$) and mixing an ethanolic solution of (0.01) mole of *m*-

amino benzoic acid with (0.01) mole of $HgCl_2$ in the same solvent. The mixture was stirred at room temperature for thirty minutes, then the residues were filtered off and the final products were recrystallized from ethanol.

Biological Study

The biological activity of the ligand (mABAH) and its metal complexes was measured using Mullar - Hiinton agar well - diffusion method and carried out for (1×10^{-3} M) solution in (DMSO) solvent [6]. The plates were incubated at 37^0C for 24 hours.

Result and Discussion

A. Elemental Analysis and Conductivity Measurements:

The elemental analysis data as well as colors and melting points for the synthesized complexes are arranged in table (1), which is consistent with the suggested stoichiometries. The molar conductances ($\Omega^{-1}.cm^2.mol^{-1}$) measurements of the synthesized complexes were carried out for (1×10^{-3} M) solution of synthesized complexes in (DMSO) solvent at 25 ºC. The obtained values are demonstrated in table (1). The molar conductivities of all synthesized complexes have non-electrolyte nature,[5].

Table (1): Color, melting point, elemental analysis and conductivity data for the synthesized *m*-aminobenzoic acid (mABAH) metal complexes.

Complexes	Compound	Color	m.p. (°C)	Found (Calculated)%			m Λ (Ω^{-1} .cm^2. mol^{-1})
				C	H	N	
	$C_7H_7O_2N$ (mABAH)	Off-white	172 - 174	61.89 (61.31)	5.07 (5.14)	10.10 (10.21)	
1	$[Cu(mABA)_2]$	Green	Dec.*	51.02(50.07)	4.01 (3.60)	8.78 (8.41)	4.6
2	$[Pb(mABA)_2]$	Off-White	Dec.*	34.61 (35.07)	2.44 (2.52)	5.76 (5.84)	3.3
3	$[Zn(mABA)_2]$	Off-White	Dec.*	49.21 (49.80)	3.66 (3.58)	8.08 (8.38)	2.6
4	$[Mn(mABA)_2]$	Off-white	355 - 360	51.72 (51.32)	3.64 (3.70)	8.40 (8.56)	4.0
5	$[Co(mABA)_2(H_2O)_2]$	Purple	355 - 360	45.69(45.79)	4.17 (4.29)	7.18 (7.54)	3.4
6	$[Cd(mABA)_2]$	Off-white	Dec.*	43.29 (43.71)	3.08 (3.17)	7.26 (7.27)	2.6
7	$[Hg(mABA)H_2OCl]$	Off-White	Dec.*	20.35 (20.65)	1.22 (1.48)	3.46 (3.43)	6.0
8	$[Ni(mABA)_2(H_2O)_2]$	Pale-green	355 - 360	45.34 (45.04)	3.97 (3.86)	7.88 (7.68)	16.11

* Decompose a above 246

B. Infra-Red Spectra:

The infrared spectra of the ligand and its metal complexes are measured in the range (200 - 4000) cm^{-1} and (400 - 4000) cm^{-1} using cesium iodide and potassium bromide discs

respectively. The characteristic band frequencies are arranged in Table (2). Figure (1- 4) shows the IR spectra of ligand and their metal complexes of Cu(II), Co(II) and Hg(II) respectively.

The band in the range of (3413 - 3500) cm^{-1} is attributed to the existence of water molecules, [6, 7]. The infrared spectrum of the complex (7) show bands at (3238 and 999) cm^{-1}, which is attribute the existence of water molecule bonded to Hg(II) complex. The infrared spectrum of the ligand (mABAH) shows band at (3550 and 3450) cm^{-1}, which are attributed to ν(N-H)asym. and ν(N-H)sym. respectively,[8]. Upon the coordination of the deprotonated ligand (mABA) to the metal centers in the complexes of (1 to 8) through its (NH_2) group without deprotonation, the ν(N-H) asym. and ν(N-H) sym vibration frequencies are shifted to lower frequencies, infrared spectrum of the ligand (mABAH), showed a broad weak band at (3413) cm^{-1}, which is attributed to ν(O-H) of the hydroxyl group of ligand. The ν(O-H) bands of complexes (1- 8) disappeared which indicate that the ligand coordinate through oxygen atom of the deprotonated ligand,[9]. The infrared spectrum of the ligand (mABAH) and the synthesized complexes showed bands in the rang (1533 – 1570) cm^{-1} and (1377 – 1392)cm^{-1}, table (2), which is attributed to ν(COO^-)asym and ν(COO^-)sym respectively, [10, 11]. Upon coordination of the carboxylic group of the ligand to the metal centers it's ν(COO^-) asym and ν(COO^-) sym vibrations shift to higher or lower frequencies,[12,13]. New bands which are not present in the spectrum of free ligand appeared at the range (538 – 595) cm^{-1}, (414 – 460) cm^{-1} and (350) cm^{-1} are attributed to ν(M-N), ν(M-O) and ν(Hg-Cl) vibrations, respectively, [14-17].

Table (2): Selected I.R. bands of the (mABAH) and its metal complexes (cm^{-1}).

Compound	ν(O-H)	ν(N-H) Asym.	ν(N-H) Sym.	ν(C-H) Aromatic	ν(COO^-) Asym.	ν(COO^-) Sym.	ν(M-O)	ν(M-N)	ν(M-Cl)
mABAH	3413 (m)	3550 (m)	3450 (w)	3100 (w)	1567 (s)	1385 (s)	-------	-------	-------
1	------	3235 (s)	3133 (s)	2927 (vw)	1570 (s)	1392 (vs)	595 (w)	460 (w)	-------
2	------	3350 (s)	3249 (s)	3056 (w)	1552 (s)	1390 (s)	561 (m)	414 (w)	-------
3	------	3271 (m)	3236 (m)	3103 (s)	1560 (s)	1398 (s)	538 (m)	541 (m)	-------
4	------	3357 (s)	3282 (s)	3029 (m)	1550 (s)	1398 (s)	557 (s)	417 (s)	-------
5	3425 (m)	3358 (s)	3282 (s)	3058 (m)	1537 (s)	1392 (s)	579 (m)	422 (m)	-------
6	------	3358 (s)	3275 (s)	3026 (w)	1533 (vs)	1387 (vs)	555 (m)	418 (m)	-------
7	3238 (b)	3332 (b)	3238 (b)	2929 (w)	1544 (s)	1377 (s)	561 (w)	420 (m)	350 (m)
8	------	3346 (s)	3276 (s)	3064 w)	1542 (m)	1390 (s)	570 (m)	428 (w)	-------

b = Broad , s= Strong , w = Weak, m =Medium, vs = Very Strong, vw = Very Weak

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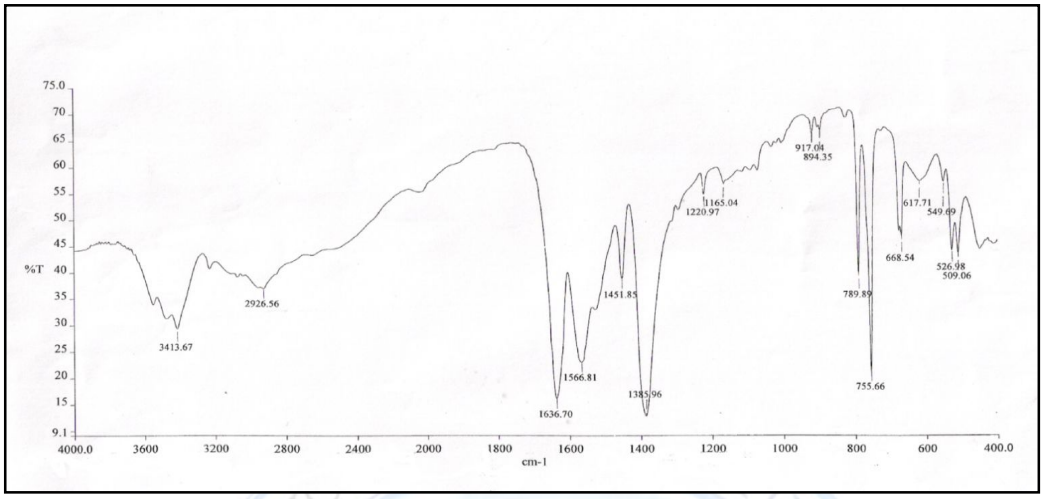

Figure (1): The Infrared Spectrum of free ligand (mABAH).

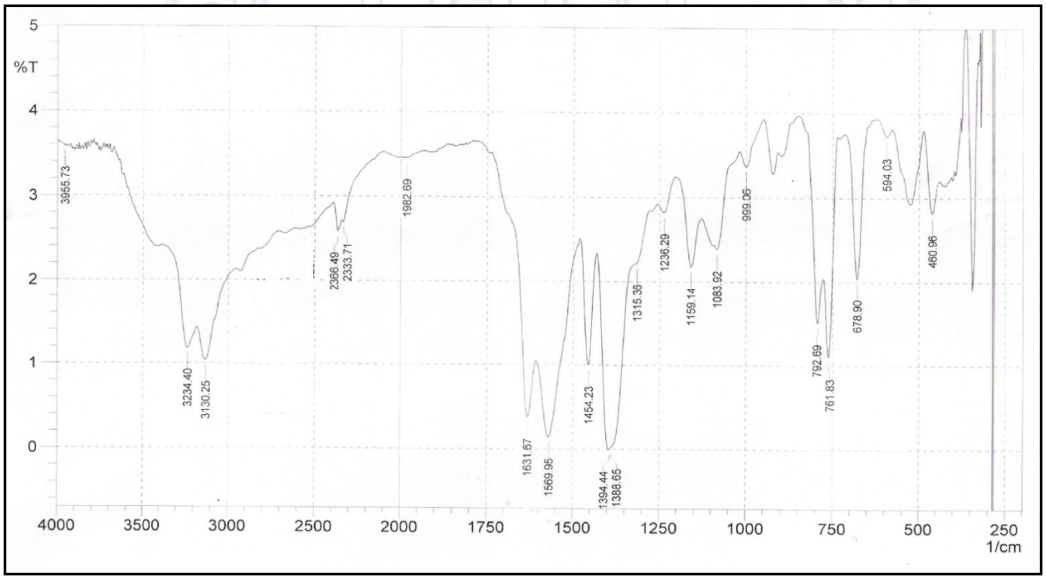

Figure (2): The Infrared Spectrum of [Cu(mABA)$_2$].

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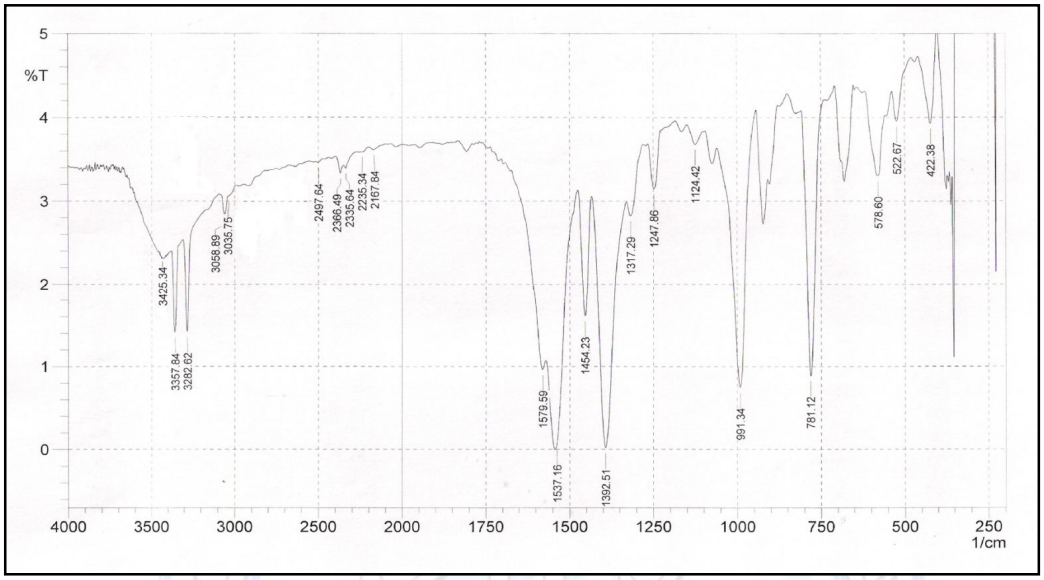

Figure (3): The Infrared Spectrum of $[Co(mABA)_2(H_2O)_2]$.

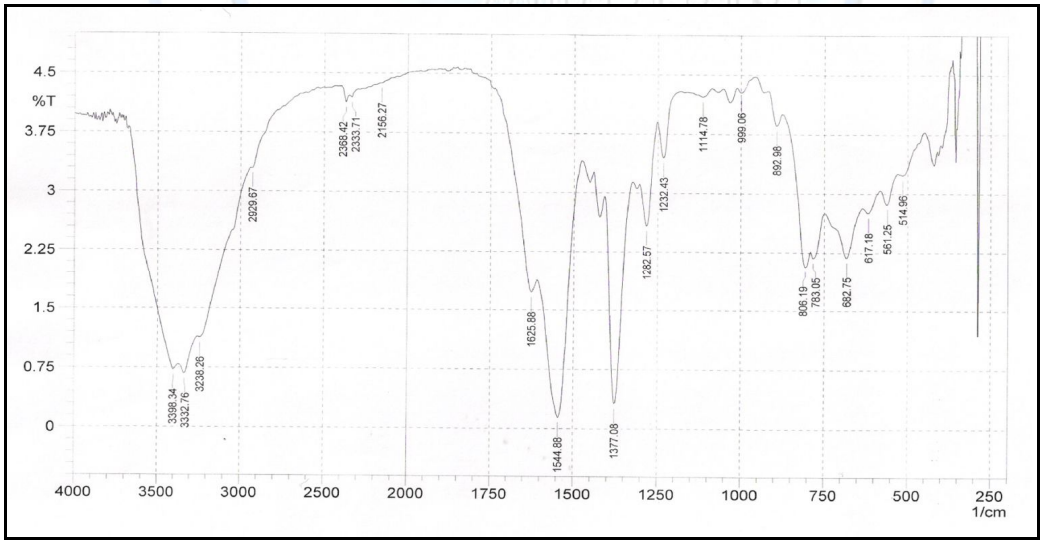

Figure (4): The Infrared Spectrum of $[Hg(mABA)(H_2O)Cl]$.

C. Electronic Spectra:

The electronic spectra of the m- amino benzoic acid and metal complexes were recorded for (DMSO) at range (200-1100) nm. The band at (36363) cm^{-1} assigned to $(\pi \rightarrow \pi^*)$ transition either for the carbonyl group or for the conjugated (π) system i.e. benzene ring and the band at (29411) cm^{-1} assigned to $(n \rightarrow \pi^*)$ transition for the nitrogen or oxygen atoms due to transferring the pair of electron from the lower energy state (n) to the higher energy state (π^*) figure (5),[18, 19].

The Cu (II) complex; (1) exhibits two bands at (29239) cm^{-1} and (21739) cm^{-1}. The band at (29239) cm^{-1} is assigned intra – ligand. While the band at (21739) cm^{-1} is attributed to ($^2T_2 \rightarrow {}^2E$) transition indicating that Cu(II)complex is distorted tetrahedral figure (6), [6, 20 - 22]. The Mn(II) complex; (4), shows two bands at (36363) cm^{-1} and (30769) cm^{-1}, which are attributed to intra – ligand and charge transfer transitions respectively ,[23]. The Co(II) complex; (5) show two bands at (38461) cm^{-1} and (30769) cm^{-1} which is assigned to intra – ligand and charge transfer transitions respectively indicating that Co(II)complex is octahedral figure (7),[24, 25]. The complexes of Pb(II), Zn(II), Cd(II) and Hg(II), complexes; (2, 3, 6 and 7) respectively, show bands in range (30769 - 47169) cm^{-1} , table (3). These complexes exhibit band above (25,000) cm^{-1} which is attributed to the (M→L) charge transfer bands indicating that complexes are tetrahedral,[21, 26 - 28]. The Ni(II) complex; (8) exhibits two bands at (38461) cm^{-1} and (31250) cm^{-1} , which are assigned to intra – ligand transition and $(^3A_{1g} \rightarrow {}^3T_{1g}(P))$ indicating that Ni(II)complex is octahedral,[29, 30].

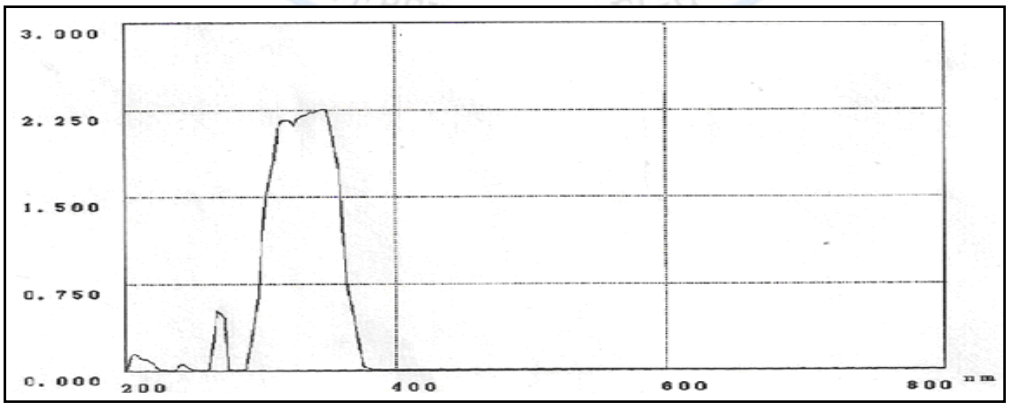

Figure (5): Electronic Spectrum of (mABAH).

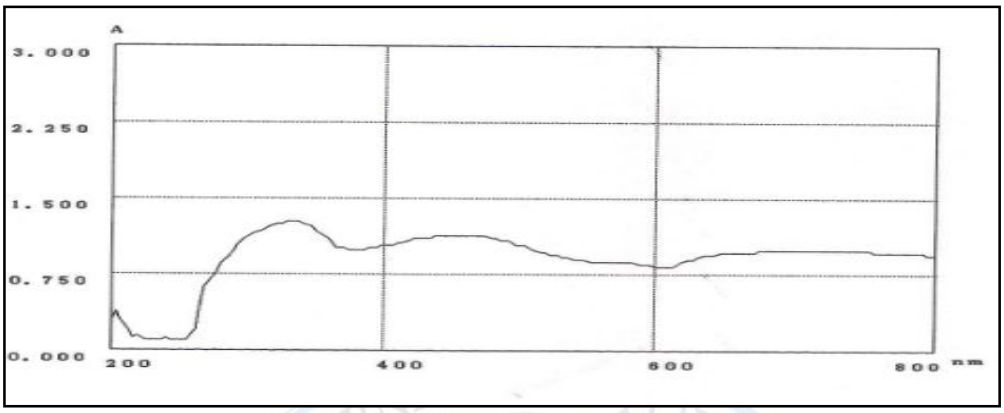

Figure (6): Electronic Spectrum of ($Cu[mABA]_2$).

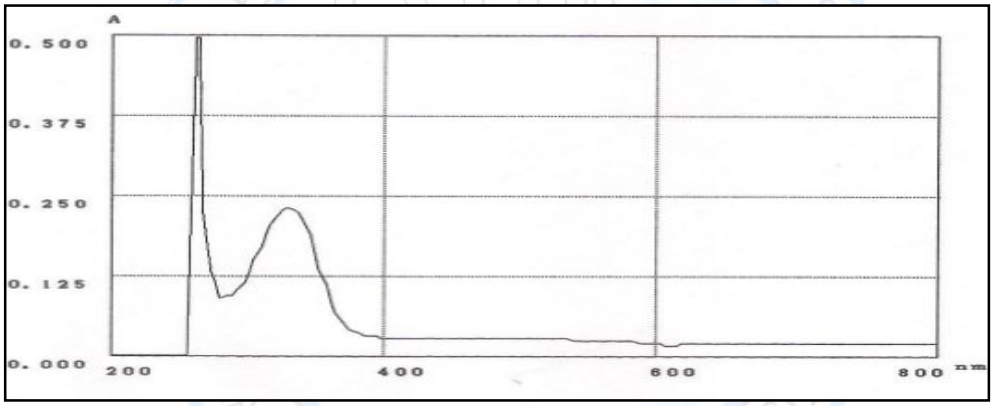

Figure (7): Electronic Spectrum of ($Co[mABA]_2(H_2O)_2$).

D. Magnetic Susceptibility:

The magnetic susceptibility of synthesized complexes are shown in Table (3). The magnetic susceptibility of the Mn(II) complex; (4), is (5.54) B.M., suggests a tetrahedral arrangement around the metal,[6]. The magnetic susceptibility of Co(II) complex; (5), is (4.98) B.M., this value refers to high spin (d^5) which suggests an octahedral geometry around the metal,[14, 29]. The magnetic susceptibility value of the prepared Ni(II) complex; (8), is (2.78) B.M. , this value refers to high spin (d^8) which suggests an octahedral geometry, [30- 32].

Table (3): Electronic spectra bands and magnetic susceptibilities for the synthesized complexes from *m*-amino benzoic acid (mABAH).

Complexes No.	Sample No.	Compounds	*Escherichia coli.* (gram negative)	*Pseudomonas aeruginosa* (gram negative)	*Staphylococcus aureus* (gram positive)
	1	mABAH	R	R	R
1	2	$[Cu(mABA)_2]$	R	R	R
2	3	$[Pb(mABA)_2]$	R	R	R
3	4	$[Zn(mABA)_2]$	R	R	R
4	5	$[Mn(mABA)_2]$	S**	S*	R
5	6	$[Co(mABA)_2(H_2O)_2]$	R	R	R
6	7	$[Cd(mABA)_2]$	S**	S*	S**
7	8	$[Hg(mABA)(H_2O)Cl]$	S**	S*	S**
8	9	$[Ni(mABA)_2(H_2O)_2]$	R	R	R

E. Biological Activity of the ligand (mABAH) and its metal complexes:

The ligand (mABAH) is resistant against these three bacteria (**Escherichia coli, Pseudomonas aeruginosa** and **Staphylococcus aureus**). The sample (5) shows very high sensitivity against **Escherichia coli.** and high sensitivity against **Pseudomonas aeruginosa**, while it is resistant against **Staphylococcus aureus.** The screened samples (7 and 8) are very high sensitivity against **Escherichia coli.** and **Staphylococcus aureus**, while they are high sensitivity against **Pseudomonas aeruginosa**, Table (4).

Table (4): Biological activity of ligand (mABAH) and its metal complexes.

	Complexes	d^n system	λ_{max} (Band absorption)		Assignment	μ_{eff} (B.M)
			cm^{-1}	nm		
	mABAH		36363 29411	275 340	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	
1	$[Cu(mABA)_2]$	d^9	29239 21739	342 460	Intra – Ligand Transition $^2T_2 \rightarrow {}^2E$	1.75 T.h
2	$[Pb(mABA)_2]$	d^{10}	47169 45454 38461 36363 30769	212 220 260 275 325	C.T. C.T. C.T. C.T. C.T.	Zero Distorted T.h
3	$[Zn(mABA)_2]$	d^{10}	36363 30769	275 325	C.T. C.T.	Zero T.h
4	$[Mn(mABA)_2]$	d^5	46511 30769	215 325	Intra – Ligand Transition C.T.	5.54 T.h
5	$[Co(mABA)_2(H_2O)_2]$	d^7	38461 30769	260 325	Intra – Ligand Transition C.T.	4,98 O.h
6	$[Cd(mABA)_2]$	d^{10}	37037 30769	270 325	C.T. C.T.	Zero T.h
7	$[Hg(mABA)(H_2O)Cl]$	d^{10}	38167 30769	262 325	C.T. C.T.	Zero T.h
8	$[Ni(mABA)_2(H_2O)_2]$	d^8	38461 31250	260 320	C.T. $^3A_{2g} \rightarrow {}^3T_{1g}$ (P)	2.78 O.h

R = Resistant, S* = Very Sensitivity, S** = High Sensitivity.

Conclusion

Based on the reported results, it may be concluded that ligand act as bidentate and monodentate ligand, coordinating through one of the nitrogen atom of amine group and through oxygen atom of the carboxylic group. According to the elemental analysis, IR, UV-Visible spectroscopy, conductivity and magnetic susceptibility data the following structures are proposed for these synthesized complexes, figure (8).

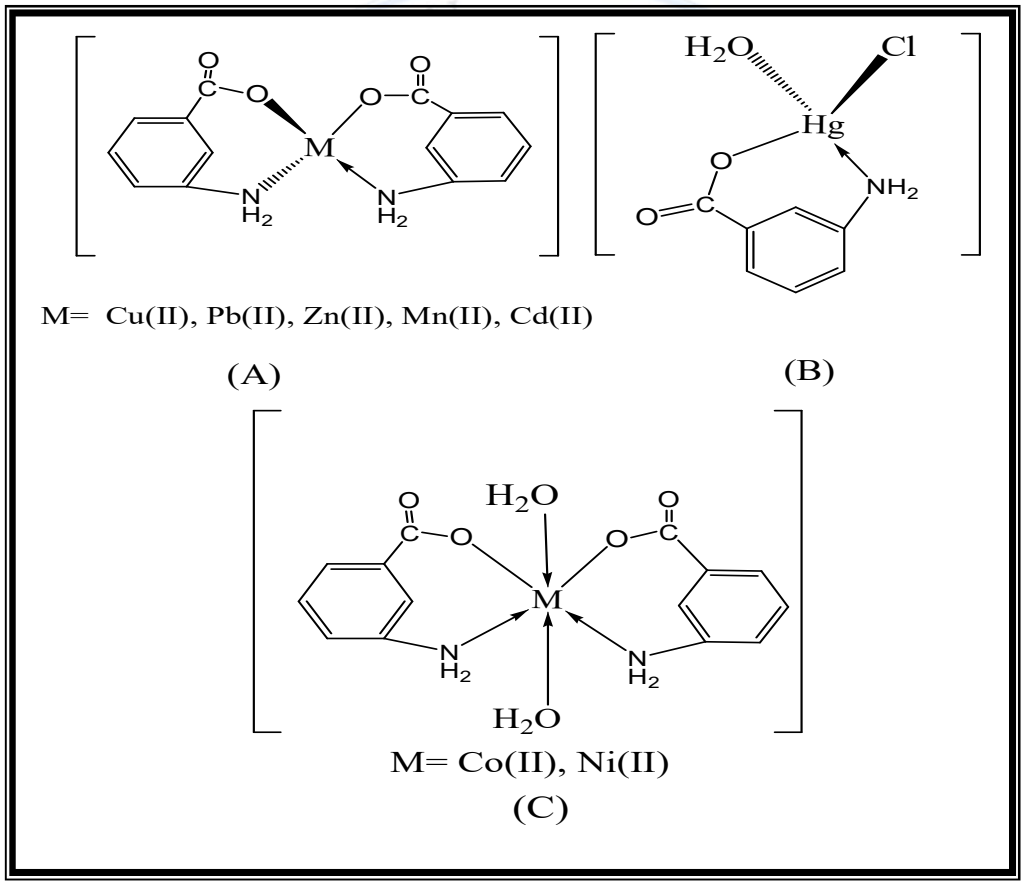

Figure (8): Proposed chemical structures for the prepared *m*-amino benzoic acid metal complexes.

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