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Synthesis, characterisation, theoretical studies and Biological activities of Mn (II), Co (II), Ni (II), Cu (II), Cr (III), Fe (III) and V (IV) Complexes with [N, N-bis (3-methyl-imidazilidene-2, 6-diamino-4-methyl pyrimidine)]

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الخلاصة:

تم في هذا البحث تحضيرقاعدة شف جديدة:

[N , N-bis (3-methyl-imidazilidene-2,6-diamino-4-methylpyrimidine](IP)

جرى تشخيص **(IP)** بطرق تحليل طيف الاشعة تحت الحمراء (FT-IR) والتحليل الدقيق للعناصر (C.H.N). استخدم **(IP)** كليكاند في تحضير معقدات الايونات الفلزية الثنائية(II) (منغنيز,الكوبلت, النيكل والنحاس) والثلاثية (III)(الكروم والحديد) و (الفناديوم)(IV).تم عزل المعقدات الجديدة وتشخيصها باستخدام طيف الاشعة تحت الحمراء وطيف الاشعة فوق البنفسجية–المرئية وتقنية (C.H.N) وتقنية الامتصاص الذري للعناصر اضافة الى قياسات الحساسية المغناطيسية والتوصيلية الكهربائية .وتم دراسة طبيعة المعقد المتكون في محلول الايثانول باتباع طريقة النسب المولية وقد اعطت هذه الدراسة نتائجا مطابقة مع تلك التي تم الحصول عليها في الحالة الصلبة،كما درست ثوابت الاستقرار للمعقدات المتكونة مع الزمن وكانت مدة ثبات اللون اكثر من (4)ساعات، فضلا عن ذلك تم حساب قيمة الممتصية المولارية للمعقدات .تضمن العمل ايضا معالجة تكوين المعقدات نظريا في الطور الغازي ،باستخدام برنامج (6-Hyperchem) وبتطبيق الميكانيك الجزيئي والشبه التجريبي في الحساب وباستخدام الدوال (PM3,ZNDO) لحساب حرارة تكوين الليكاندت والمعقدات (ΔH_f) وطاقة التاصر (ΔE_b) و أطوال الأواصر (ΔE_L) وبدرجة حرارة 298 كلفن وقد وجد ان جميع المعقدات المحضرة مستقرة وهذه النتائج تتفق مع النتائج التي تم الحصول عليها عمليا من قيم ثابت الاستقرارية في المحلول . كذلك تم حساب الجهد الكهروستاتيكي لليكاند(IP) لتحديد المواقع الفعالة ضمن الجزيئة .جرى كذلك حساب قيم الاطياف الاهتزازية والاطياف الالكترونية لليكاند

(IP) ومعقداته نظريا باستخدام PM3 ومقارنتها مع القيم المقاسة عمليا,ووجد بان هنالك توافقا كبيرا بين القيم العملية والمحسوبة نظريا .

تمَّ تقويم الفعالية المضادة للبكتريا لليكاند **(IP)** ومعقداته وأُختير نوعان من البكتريا (*Pseudonomous aerugionosa*) سالبة الصبغة و (*Bacillus Subtilis*) موجبة الصبغة لهذا الغرض كما تم اجراء التقويم الحيوي لليكاند **(IP)** ومعقداته ضد نوعين من الفطريات (*Penicillum Spp.* و *Aspergillus flavus*) وقد أظهرت نتائج التقويم زيادة كبيرة في فعالية المعقدات المحضرة منها.

Abstract:

A new Schiff base [N,N^--bis(3-methyl-imidazilidene-2,6-diamino-4-methyl pyrimidine], (IP) have been prepared and characterized by (FT-IR) Spectroscopy and elemental analysis (C.H.N) .(IP) has been used as a chelating ligand to prepare some complexes of (Mn(Π),Co(II), Ni(Π), Cu(Π), Cr(Ш), Fe(Ш) and V(IV) ions .The prepared complexes were identified and their geometrical were suggested in solid state by using (FT-IR) and (UV-Vis) spectroscopy ,elemental analysis(C.H.N), Flame atomic absorption technique, in addition to magnetic susceptibility and conductivity measurements .The study of the nature of the complexes formed in ethanol following the mole ratio method, gave result which were compared successfully with those obtained from solid state studies . The apparent stability constant of the complexes have been studied with the time and their color were stable for more than (4hours), as well as the molar absorptivities have been calculated.

The work also include a theoretical treatment of the formed complex in the gas phase, this was done using the hyperchem-6 program for the molecular mechanics and semi-empirical calculations .The heat of formation ($\Delta H_f°$), binding energy (ΔE_B) and bond length (ΔE_L) for ligand (IP) and its metal complexes were calculated by (PM3 and ZNDO\1) methods at 298 K°.It was found that the ligand (IP) and it s metal complexes were stable, which agreed well with the experimental stability constants in solution. Further more the electrostatic potential of the free ligand was calculated to investigate the reactive sites of the molecules .PM3 were used to evaluate the vibrational spectra and electronic spectra of the ligand (IP)and it's metal complexes then comparing with the experimental values .The theoretically obtained agreed with those found experimentally. The antibacterial activity for free ligand (IP) and their metal complexeswere studied against two selected micro - organisms *[(Pseudonomous aerugionosa) as gram negative]* and*[(Bacillus Subtilis) as gram positive]*. Further more the antifungal activity against two micro-organism *(Penicillum Spp.)* and *(Aspergillus flavus)* were studied for all compounds. The results showed great enhancement of activity of the complexes relative to that of their respective free ligand (IP).

Introduction:

The pyrimidine ring system, present in nucleic acids, several vitamins, coenzymes and antibiotics (1, 2), etc., provides potential binding sites for metal ions, and any information on their coordinating properties is important as a means of understanding the role of the metal ions in biological systems (3-6). Many compounds of therapeutic importance contain pyrimidine ring system such as: Sulphadiazin, a sulphonamide of **(2-amino pyrimidine and trimethoprim)**, which are antibiotics (1, 7).

The present paper describe the preparation of a new (IP) ligand derived from the 2,6-diamino-4-methylpyrimidin heterocyclic ring and 2-oxo-3-methyl imidazole, was described in an attempt to introduce the azomethine moiety in the structure of pyrimidine ring with the ion pair of electrons on the nitrogen atom that provides four potential donor sites to investigate the coordination behavior of the new ligand toward some transition metal ions as well as to compare the theoretical studies of the (IP) ligand and their metal complexes with experimental results.

Experimental:

(A)Physical measurements and analysis:

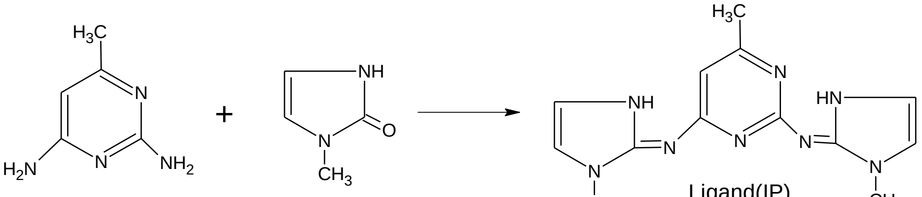
Melting points were recorded on gallenkamp Melting point apparatus and were uncorrected. FT-IR spectra were recoded using FT-IR8300 Schimadzu in the range of (4000-200) cm^{-1}, samples were measured as (CsI disc).Electronic spectra were obtained using UV-1650PC Schimadzu Spectrophotometer at room temperature, the measurements were recorded using a concentration of 10^{-3} M of the complex in chloroform as a solvent. The metal content was estimated spectrophotometerically using atomic absorption Schimadzu AA670 Spectrophotometer. The elemental analyses (C.H.N) were obtained using EA-034.mth. Conductivity measurements were obtained using Corning conductivity meter 220, these measurements were obtained in DMF solvent using concentration of (10^{-3} M) at 25C°.Magnetic susceptibility measurements were obtained at 25C° on the solid state applying Faraday's method using Bruker BM6 instrument.

(B)Material and Methods:

All chemicals were of highest purity and were used as received.

Preparation of the ligand (IP):

To a hot ethanolic solution of (2,6-diamino-4-methyl pyrimidine) (0.015 mole,2.28gm),a solution of (2-oxo-3-methyl imidazole (0.03 mole,5.88gm) in (25ml)ethanol was added with catalytic amount of glacial acetic acid, the reaction mixture was refluxed for (5 hours). On cooling the separated solid was filtered and recrystallized from ethanol, yield 80% , melting point of the prepared product are listed in table (1).



Preparation of the metal ion complexes (D1-D7):

Ethanolic solution of each of the following metal ion salts (0.52 mmole) [$MnCl_2.2H_2O$, $CoCl_2.6H_2O$, $NiCl_2.6H_2O$,$CuCl_2.2H_2O$,$CrCl_3.6H_2O$.$FeCl_3.9H_2O$ and $VOSO_4.5H_2O$] was added to an ethanolic solution (1.15 mmole) of (IP) with stirring. The mixture was heated under reflux for (1hour), during this time the precipitate of the complexes was formed. The product was filtered off, washed with hot ethanol, followed by cold water and then dried under vacuum.

Study of complex formation in solution:

Complexes of (IP) with metal ions were studied in solution using ethanol as a solvent, in order to determined (M:IP) ratio in the complex following molar ratio method(8).A series of solutions were prepared having a constant concentration [10^{-3}M] of the metal ion and (IP). The [M/(IP)] ratio was determined from the relationship between the absorption of the absorbed light and the mole ratio of [M: (IP)].The results of complexes formation in solution were listed in Table(1).

Stability constant of Schiff base complexes:

The conditional (8) stability constant of the (1:1) [Metal: ligand] complex were evaluated as fallows:

Two sets of solutions were prepared, the first set of solution (As)were formulated to contain stoichiometric amount (1ml) of (10^{-3}M) ligand to (1ml)of (10^{-3}M) of metal ion by placing in to a three series of (10ml) volumetric flasks. The solutions of the coloured complexes were diluted to the mark with ethanol. The second set (Am)were formulated to contain five fold excess (5ml) of (10^{-3}M) ligand, by placing in to a three series of (10ml) volumetric flasks followed by addition of (1ml) of (10^{-3}M)of metal ion solution, the volumes were then completed to the mark with ethanol. The absorbance (As and Am) of the solutions were measured at (λ_{max}) of maximum absorption. The stability constant (k) and the molar absorptivity (ε_{max}) have been calculated.

<u>Theoretical treatment:</u>

Hyperchem is a sophisticated molecular modeler, editor and powerful computational package, that is known for its' quality, flexibility and ease of use (9, 10a). It can plot orbital wave functions resulting from semi-empirical quantum mechanical calculations, as well as the electrostatic potential, the total charge density or the total spin density can also be determined during semi-empirical calculation, this information is useful in determining reactivity and correlating calculation results with experimental data.

-Computational methods:

a) Semi -empirical quantum mechanical
b) Molecular mechanics
c) Mopac 2000

Hyperchem offers ten semi -empirical molecular orbital methods, with options for organic and main group compounds, for transition metal complexes and for spectral simulation. Choose from Zerner's INDO Method (ZENDO/1) and Parameterization Model version 3 (PM3) including transition metals (10a,b).

-Types of calculations:

The types(9, 10a,b) of prediction possible of Molecules are:

a) Geometry optimization calculations employ energy minimization algorithms to locate stable structures.
b) Bond distances
c) Molecular dynamics witch provide the thermodymemic calculations and dynamic behavior of molecules
d) Plot the electrostatic potential field (HOMO and LUMO).
e) Vibrational spectrum (I.R and Raman spectra).
f) Electronic spectrum (U.V- Visible spectra).

Study of biological activities for (IP) ligand and (D1 – D7) their metal complexes

The ***in vitro*** biological screening effects of the investigated compounds were tested against selected types of bacteria which include ***(Pseudonomous aerugionosa)*** as gram negative **and** ***(Bacillus Subtilis)*** as gram positive and the fungus, *(Penicillum Spp.)* and *(Aspergillus flavus)* by the well diffusion method using Nutrient agar as method(11). Stock solutions (10^{-3}M) were prepared by dissolving the compounds in DMSO solution. In a typical procedure, a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using a micropipette and the plat was incubated at

30 C$^\circ$ for 72 hours. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected.

Result and discussion:

Part (I):- Synthesis and characterization of the isolated schiff base derivatives of 2, 6-diamino-4-methyl pyrimidine

(A)Elemental analysis:

The physical and analytical data of (IP) and its metal complexes are given in table (1); they are in a satisfactory agreement with the calculated values. The suggested molecular formulas also supported by spectral and elemental analysis as well as magnetic susceptibility and conductivity measurements.

Table (1)
Physical data for (IP) and it's metal complexes

Comp. No.	***Color***	***Melting point***	***Yield %***	***Metal analysis found (calc.)***				***Suggested formula for isolated precipitate***
				C%	***H%***	***N%***	***M%***	
(IP)	Yellow	142-145	88	55.14 (54.93)	5.07 (5.63)	39.75 (39.43)	–	$C_{13}H_{16}N_8$
(D1)	Light brown	161	86	38.98 (39.48)	4.27 (4.83)	25.3 (24.56)	11.89 (12.05)	$[Mn(IP)Cl_2].C_2H_5OH$
(D2)	Brown	168	78	36.88 (37.87)	8.03 (7.88)	27.31 (27.19)	17.64 (17.82)	$[Co(IP)Cl_2]$
(D3)	Brown	175	80	35.47 (36.14)	5.01 (4.17)	26.25 (25.94)	12.94 (13.59)	$[Ni(IP)Cl_2].H_2O$
(D4)	Green	163	84	37.33 (37.27)	4.46 (3.82)	25.91 (26.96)	15.23 (15.18)	$[Cu(IP)]Cl_2$
(D5)	Deep Green	188	72	32.06 (31.52)	3.68 (4.43)	23.24 (22.56)	16.68 (17.47)	$[Cr(IP)Cl_2]Cl.3H_2O$
(D6)	Red-Brown	184	70	33.12 (32.34)	3.26 (4.15)	22.48 (23.22)	12.29 (11.58)	$[Fe(IP)Cl_2]Cl.2H_2O$
(D7)	Greenish-blue	173	82	34.62 (34.90)	2.86 (3.58)	24.93 (25.06)	10.47 (11.39)	$[VO(IP)]SO_4$

Infrared Spectra:

In Order to study the binding mode of the schiff base to the metal ion in the complexes, the FT-IR spectrum of the free ligand (IP) was compared with the spectra of the complexes. The FT-IR spectrum of the ligand shows bands in the regions (3244),(2866,2978) and (1645) cm^{-1},which are assigned to [υN-H, υN-CH3 and υC=N] respectively (12,13) .In all complexes the ligand (IP) behave as tetradentate coordinating with the metal ions through nitrogen of the azomethine (υC=N) and nitrogen of the -3- methylimidazole ring (υN-CH_3)$_3$ which shifted to lower frequencies , (table 2), while the band related to (υ N–H) vibration was still unchanged , (table 2). These observations were further indicated by the appearance of (υ M-N and υM-Cl) respectively (14), (table 2). As well as a strong band was observed at (975) cm^{-1} due to (υV=0) stretching mode in (D7) complex (10, 11). The band related to sulfate anion in the (D7) complex were observed at (1015, 1260 and 1470) cm^{-1} indicated a free anion (14). Abroad band was observed around (3455-3515) cm^{-1} in the spectra of [D1, D3, D5 and D6] complexes, assigned to a (υO-H) and suggested the presence of a water or ethanol molecules in the complex (13, 15).

Table (2)

Characteristic stretching vibrational frequencies (cm^{-1}) located in the FT-IR spectra of (IP) and itś metal complexes

Comp. No.	*υC=N*	*υ N-CH3*	*υ N-H*	*υ M-N*	*υ M-Cl*	*υ O-H*
(IP)	1645(s)	2866,2978(s)	3244(sb)	-	-	-
(D1)	1633(m)	2850,2967(m)	3242(sb)	503,510(mw)	405(w)	3515(b)
(D2)	1639(m)	2850,2967(m)	3244(sb)	501,507(mw)	408(w)	-
(D3)	1634(m)	2853,2965(m)	3242(sb)	503,510(mw)	403(w)	3450(b)
(D4)	1633(m)	2850,2967(m)	3250(sb)	506,511(mw)	406(w)	-
(D5)	1633(m)	2850,2965(m)	3242(sb)	503,510(mw)	405(w)	3455(b)
(D6)	1637(m)	2852,2960(m)	3244(sb)	505,511(mw)	406(w)	3452(b)
(D7)	1639(m)	2854,2968(m)	3242(sb)	501,510(mw)	-	-

Where :- (s=strong, m=medium sb=strong broad, mw=medium week, w =week, b=broad)

Electronic absorption Spectra, Magnetic susceptibility and Conductivity measurement:

Table (3) gives the electronic spectra of the metal complexes were recorded for their solution in chloroform, in the range (200-1100) nm, and magnetic moments at room temperature as well as the molar conductance values of the complexes in (DMF).

The **(IP)** ligand exhibit two bands around 34000 and 30000 cm^{-1}, these intense bands are due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions respectively(13).

(D1) :- Electronic spectra of Mn(II) complex showed very weak absorption bands, which are not of any help in assigning the geometry(16) , this is expected because the only sextet term of the

[d^5] configuration in octahedral stereochemistry(17,18) and showed bands at (17857,22999 and 26490)cm^{-1} , which are assigned to the transitions :
$^6A_1g \rightarrow ^4 T_1g$ (G) $^6A_1g \rightarrow ^4Eg$, ^4A_1g (G) and $^6A_1g \rightarrow ^4T_2g$ (G) respectively (18). The values of racah parameters (10Dq,B$^-$ and β) have been calculated to be (9987,803 and 0.94)respectively(18,19) .Magnetic moment of the solid complex (5.93 B.M) showed a high spin Mn(II) complex(20-22). Conductivity measurement showed the complex was non ionic, table (3).

(D2):- Two absorption bands were observed in the spectrum of this complex at (19685 and 21978) cm^{-1} and were assigned to $^4T_1g \rightarrow ^4A_2g$ (F) (υ_2) and $^4T_1g \rightarrow ^4T_1g$ (p) (υ_3) respectively of octahedral Co (II) complexes (23-27) . The value of (υ_1) related to the transition $^4T_1g \rightarrow ^4T_2g$ (F), was obtained by applying the ratio of (υ_3/υ_2) on Tanaba Saugano diagram of Co(II) complexes(24,26) and was found to be (10963cm^{-1}) . The ratio of (υ_2 /υ_1) (1.79) indicated a distorted octahedral complex (25,28) . The value of nephelauxetic ratio (0.93) showed some degree of covalancy (26). The magnetic moment (5.08B.M) indicated a high spin octahedral complex (20). Conductivity measurement showed that complex was non ionic table (3) .

(D3):- The electronic spectra of the brown complex is consistent with octahedral geometry showing two main absorption bands at 16225 and 25000cm^{-1} , which are assignable to the transitions, $^3A_2g \rightarrow ^3T_1g$ (F)(υ_2) and $^3A_2g \rightarrow ^3T_1g$ (P)(υ_3) respectively(26,28). The calculated values of (Dq,B,β, υ_1 and υ_2 /υ_1) have been calculated to be (1065.1,554.2 ,0.56 ,10651 and 1.52) respectively. The (β) value signifies a fair amount of covalent character in metal to nitrogen of azomethine and nitrogen of amino methyl bonds, while the value of (υ_2 /υ_1) (1.52)is less than (1.8) it suggest to lie in the same range as reported for octahedral coordinated Ni(II) ion(26,28) . The value of (υ_1) related to the transition $^3A_2g \rightarrow ^3T_2g$ (F) and corresponds to (10Dq), was obtained by applying the ratio of υ_3 /υ_2 on Tanaba Saugano diagram of Ni (II) complexes (28,29). The magnetic susceptibility (3.38B.M) at room temperature consistent with the spin-free octahedral geometry around the Ni (II) ion (20, 22, 30).Conductivity measurement in Table (3) showed that the complex was non ionic.

(D4):- The UV-Vis spectrum of Cu (II) complex in ($CHCl_3$) solution displays intense bands at (11059, 14722 and 20191) cm^{-1} assign to (d-d) electronic transition type $^2B_1g \rightarrow ^2A_1g$, $^2B_1g \rightarrow ^2B_2g$ and $^2B_1g \rightarrow ^2Eg$ respectively(23,34) , which strongly favor square planar geometry around the central metal ion (28, 31) . The high energy band at 28897 cm^{-1} may be assigned to ligand-metal charge transfer transition (31). This is further supported by the magnetic susceptibility value (1.82B.M), which agree well with square planar structure (30).Conductivity in (DMF) solution, table (3) showed that the complex was highly conducting, therefore the **(Cl)** ion wasn't considered to be coordinated with metal ion and is located outside the coordination zone.

(D5):- Three absorption bands were observed in the spectrum of this complex at (13021, 15997 and 31018) cm^{-1} assign to (d-d) electronic transition type $^4A_2g \rightarrow ^2T_2g$, ^2Eg , $^4A_2g \rightarrow ^4T_2g(F)$ and $^4A_2g \rightarrow ^4T_1g(P)$ which confirms octahedral geometry (28, 31). This is further confirmed by its magnetic susceptibility value (3.86 B.M) Conductivity showed that the complex was to be electrolyte, table (3).

(D6):- This complex showed three bands related to octahedral iron complex (19, 23, 32-34). They were observed at (16129, 18052 and 29412) cm^{-1} and were assigned to the transitions: $^6A_1g \rightarrow ^4T_1g$ (G), $^6A_1g \rightarrow ^4Eg, ^4A_1g$ and $^4A_1g \rightarrow ^4T_2g(4E)$ (23,34). The values of (10Dq, B and β) came out to (7089, 595 and 0.45) respectively. The magnetic moment is (5.75 B.M.) indicated a high spin octahedral complex (20, 22, 34) . Conductivity in (DMF) showed that the complex was ionic, table (3).

(D7):- The spectrum of vanadyl (IV) complex show two main absorption bands, table (3), which are assigned to the two transition $^2B_2 \rightarrow ^2E$ and $^2B_2 \rightarrow ^2B_1$ respectively in a square pyramidal geometry(24,28) . The magnetic moment (2.03 B.M) is higher than spin value of the vanadium metal only, this result indicate a higher orbital contribution (24, 28, 35) . Conductivity measurement in (DMF) showed that the complex was ionic, Table (3).

Table (3)
Electronic spectra ($CHCl_3$), Magnetic moment (B.M) and Conductance in (DMF) for metal complexes

Comp. No.	*Bands cm^{-1}*	*Assignment*	*10Dq*	*Molar cond. $\mu s.\ Cm^{-1}$*	*μeff. B.M*	*Suggested structure*
(D1)	17857 22999 26490	${}^{6}A_{1}g \rightarrow {}^{4}T_{1}g(G)$ ${}^{6}A_{1}g \rightarrow {}^{4}Eg, {}^{4}A_{1}g(G)$ ${}^{6}A_{1}g \rightarrow {}^{4}T_{2}g(4E)$	9987	12.87	5.94	Octahedral
(D2)	10963(Calc.) 19685 21978	${}^{4}T_{1}g \rightarrow {}^{4}T_{2}g(F)$ ${}^{4}T_{1}g \rightarrow {}^{4}A_{2}g(F)$ ${}^{4}T_{1}g \rightarrow {}^{4}T_{2}g(P)$	10963	10.51	5.08	Octahedral
(D3)	10651(Calc.) 16225 25000	${}^{3}A_{2}g \rightarrow {}^{3}T_{2}g(F)$ ${}^{3}A_{2}g \rightarrow {}^{3}T_{1}g(F)$ ${}^{3}A_{2}g \rightarrow {}^{3}T_{1}g(P)$	11569	18.34	3.38	Octahedral
(D4)	11059 14722 20191 28897	${}^{2}B_{1}g \rightarrow {}^{2}A_{1}g$ ${}^{2}B_{1}g \rightarrow {}^{2}B_{2}g$ ${}^{2}B_{1}g \rightarrow {}^{2}Eg$ (IP) $\rightarrow$ Cu(C.T)	11059	177	1.81	Square planar
(D5)	13021 15997 31018	${}^{4}A_{2}g \rightarrow {}^{2}T_{2}g, {}^{2}Eg$ ${}^{4}A_{2}g \rightarrow {}^{4}T_{2}g(F)$ ${}^{4}A_{2}g \rightarrow {}^{4}T_{1}g(P)$	-	71.03	3.86	Octahedral
(D6)	16129 18052 29412	${}^{6}A_{1}g \rightarrow {}^{4}T_{1}g(G)$ ${}^{6}A_{1}g \rightarrow {}^{4}Eg, {}^{4}A_{1}g(G)$ ${}^{6}A_{1}g \rightarrow {}^{4}T_{2}g(G)$	7089	68.29	5.75	Octahedral
(D7)	11740 17228	${}^{2}B_{2} \rightarrow {}^{2}E$ ${}^{2}B_{2} \rightarrow {}^{2}B_{1}$	-	74.68	2.03	Square Pyramidal

Part (II):- Spectrophotometer study of complex formation in organic solvent

(1)-Molar ratio method:

The compositions of the (D1-D7) complexes have been studied by the molar ratio method. The results of complexes in ethanol as a solvent, suggest that the metal to ligand ratio was (1:1) for all complexes, which were comparable to those obtained from solid state study, table (4).

(2)-Stability constant of the Schiff base complexes:

The apparent stability constant of the (1:1) [Metal: Ligand] complexes was estimated, table (4).

The average of three measurements of the absorption of solution containing a stoichiomtetric amount of ligand and metal ions (As), while the (Am) equal the average of three measurements of the absorption of solution containing the same amount of metal and five fold excess of ligand of the solutions, were measured at λmax of maximum absorption, as well as the degree of dissociation (α) and molar absorptivity (ε_{max}) for all complexes were calculated [(8)], Table (4). The results indicate that (D1-D3-D5 and D6) complexes yielded rather high stability in contrast to the other values obtained with (D4 and D7) , this refer to their structural geometric, table(4). Furthermore the (ε_{max}) of all complexes is rather high, this probably due to the presence of methyl group on the nitrogen atom, table (4). The developed colors become stable after one hour, up to four hours.

Table (4)

Molar ratio, Stability constant and molar absorptivities of Schiff base complexes at room temperature

Complex	*M:(IP) Ratio*	*As*	*Am*	*α*	*K L.mol $^{-1}$*	*ε max L.mol.cm^{-1}*	*λ max nm*
(D1)	1:1	0.380	0.459	0.128	$6.49*10^5$	4532	415
(D2)	1:1	0.441	0.496	0.111	$7.23*10^5$	4960	500
(D3)	1:1	0.369	0.458	0.194	$6.144*10^5$	4580	504
(D4)	1:1	0.217	0.354	0.137	$2.58*10^5$	3541	495
(D5)	1:1	0.458	0.497	0.039	$8.06*10^5$	4976	639
(D6)	1:1	0.496	0.585	0.089	$7.64*10^5$	5853	545
(D7)	1:1	0.377	0.439	0.135	$6.09*10^5$	4396	751

(As)= The average of three measurements of the absorption of solution containing a stoichiomtetric amount of ligand and metal ions.

(Am)= The average of three measurements of the absorption of solution containing the same amount of metal and five fold excess of ligand of the solutions.

Part (III):- Theoretical study of Schiff base and their metal complexes in gas phase

A) Optimized geometries and energies:

The conformations of the ligand and complexes obtained from molecular mechanics calculation were fully re-optimized to estimate the binding energy and the enthalpies of formation for the ligand and complexes by using the PM3 semi-empirical method at a value of Geometry Optimization constant (0.01Kcal/mol) for the ligand and their metal complexes, as is shown in Table (5) .

Table (5)
Conformation energetic in (Kj. mol^{-1}) for Schiff base and their metal complexes

Conformation	ΔHf^{o}	ΔEb
(IP)	129.57	-3850.47
(D1)	-89.58	-3995.29
(D2)	-97.03	-4216.6
(D3)	-167.31	-3545.39
(D4)	-69.78	-3599.87
(D5)	-217.91	-3894.26
(D6)	-64.15	-4180.3
(D7)	-81.69	-12408.1

B) Electrostatic Potentials:

Electron distribution governs the electrostatic potential of the molecules. The electrostatic potential (E.P) describes the interaction of energy of the molecular system with a positive point charge. (E.P) is useful for finding sites of reaction in a molecule; positively charged species tend to attack a molecule where the electro static potential is strongly negative (electrophonic attack)(36) . The (E.P) of the free ligand (IP) was calculated and plotted as 2D contour to investigate the reactive sites of the molecules, Fig (1). Also one can interpret the stereochemistry and rates of many reactions involving “soft” electrophiles and nucleophiles in terms of the properties of frontier orbital (HOMO, highest occupied molecular orbital) and (LUMO, lowest unoccupied molecules). The results of calculations show that the LUMO of transition metal ions prefer to react with the HOMO of **(C=N)** and **(-N-CH_3)** for **(IP)** ligand.

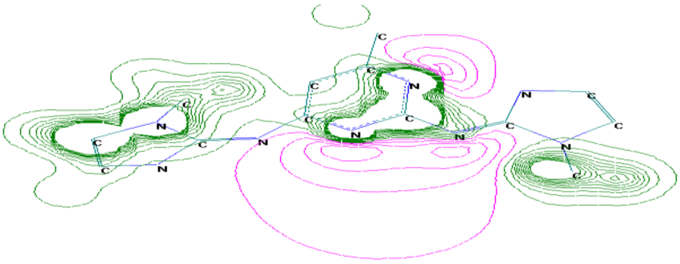
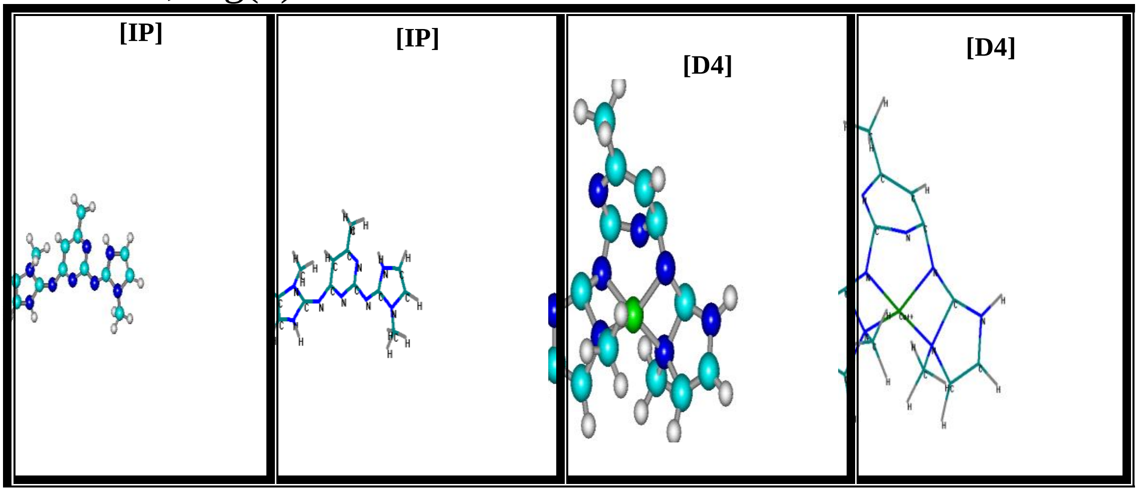


Fig. (1):- electrostatic potential (HOMO and LUMO) as 2D contours for Schiff base (IP)

C) Optimized geometries of (IP) and their metal complexes (D1-D7):

All theoretically probable structures of (IP) schiff base and their metal complexes have been calculated by PM3 method in gas phase to search for the most probable model building stable structure , Fig(2) .



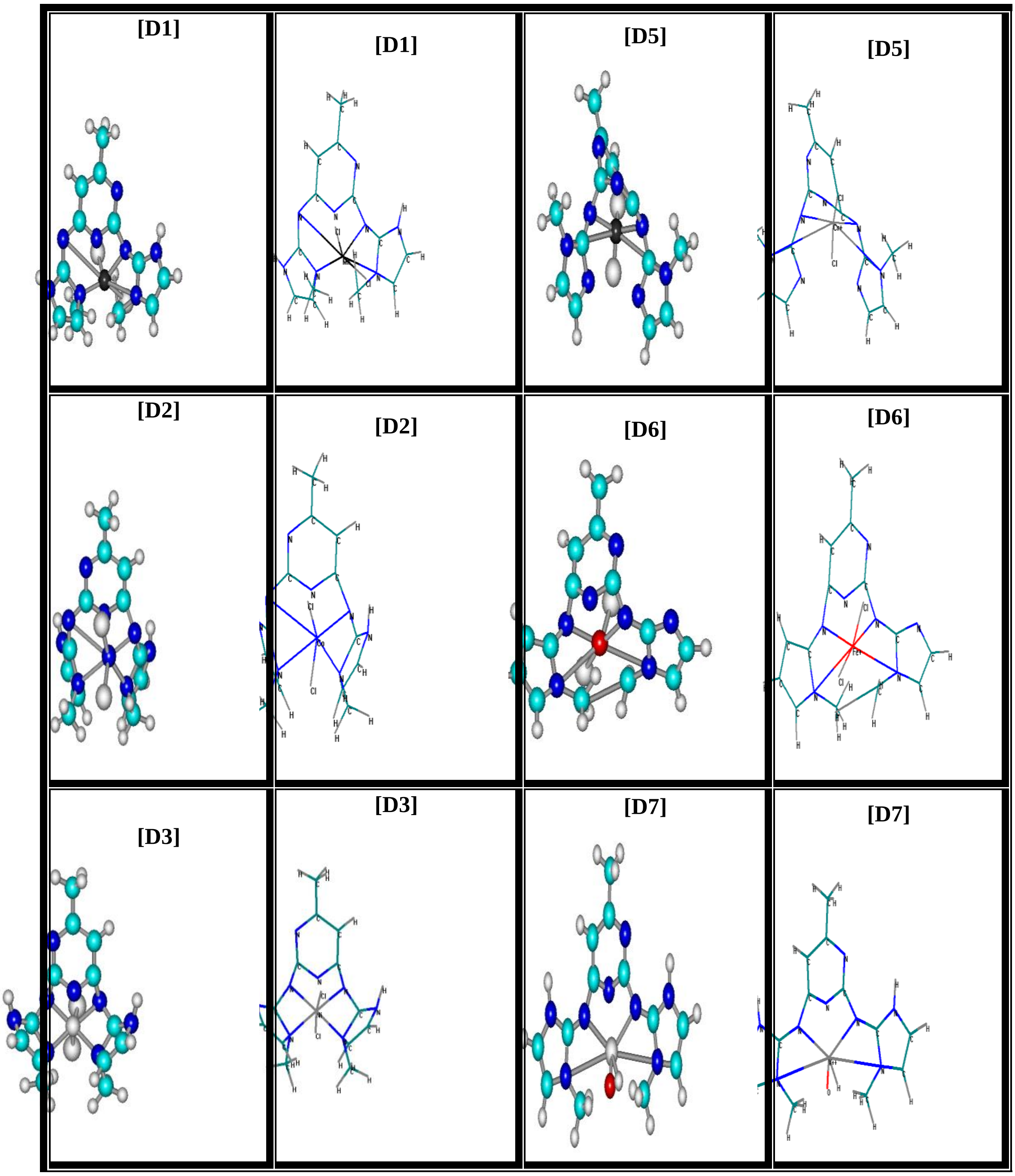


Fig:-(2) Conformational Structure of (IP) and their metal complexes (D1-D7)

***D) Optimized vibrational spectra for (IP) and their metal complexes*:**

The vitrational spectra of the free ligand (IP) and their metal complexes (D1-D7) have been calculated, Table (6). The theoretically calculated wave numbers for (IP) and (D1-D7) compounds showed that some deviations from the experimental values, these deviations are generally acceptable in theoretical calculations (37). The most diagnostic calculated vibrational frequencies were chosen for the assignment of (IP) ligand and (D1-D7) metal complexes which are included in Table (6), and their respective experimental vibrational modes are shown in Table(2).

The results obtained for the theoretical calculations of the frequencies of υ(C=N), υ(N-CH3) and υ(N-H) for (IP) ligand and (D1-D7) complexes as well as υ(M-N), υ(M -Cl) and υ(O-H) which agreed well with those obtained with the experimental values in Table(2) .

The theoretical frequencies help us to predict the most stable structure among the probable structures of ligand and their metal complexes.

Table (6)
Comparison between the experimental and theoretical vibational frequencies for (IP) ligand and (D1-D7) complexes (cm^{-1})

Comp. No.	***υ C=N***	***υ N-CH3***	***υ N-H***	***υ M-N***	***υ M-Cl***	***υ O-H***
(IP)	(1652)*	(2858,2970)*	(3240)*	-	-	-
	(1645)**	(2866,2978)**	(3244)**	-	-	-
	[0.426]***	[0.27,0.26] ***	[0.123] ***			
(D1)	(1637)*	(2856,2968)*	(3239)*	(497,517)*	(430)*	(3522)*
	(1633)**	(2850,2967)**	(3242)**	(503,510)**	(405)**	(3515)**
	[0.245] ***	[0.211,0.034] ***	[0.093] ***	[1.19,1.37] ***	[6.17] ***	[0.19] ***
(D2)	(1640)*	(2857,2960)*	(3230)*	(483,502)*	(409)*	-
	(1639)**	(2850,2967)**	(3244)**	(501,507)**	(408)**	-
	[0.06] ***	[0.25,0.24] ***	[0.43] ***	[3.59,0.96] ***	[0.24] ***	-
(D3)	(1638) *	(2849,2960)*	(3250)*	(496,513)*	(406)*	(3448)*
	(1634)**	(2853, 2965)**	(3242)**	(503, 510)**	(403)**	(3450)**
	[0.026]***	[0.014,0.016]***	[0.224]***	[0.013,0.019]***	[0.007]***	[0.059]***
(D4)	(1630)*	(2846,2959)*	(3241)*	(499, 509)*	(405)*	-
	(1633)**	(2850,2967)**	(3242)**	(506, 511)**	(406)**	-
	[0.18] ***	[0.14,0.26] ***	[0.031] ***	[0.13,0.39] ***	[0.26] ***	-
(D5)	(1645)*	(2836, 2966)*	(3240)*	(498, 515)*	(409)*	(3448)*
	(1633)*	(2850, 2965)**	(3242)**	(503,510)**	(405)**	(3455)**

	*					
	[0.73]***	[0.49 ,0.034]***	[0.062]***	[0.99 ,0.98]***	[0.99]***	[0.20]***
(D6)	(1643)*	(2825,2964)*	(3244)*	(498,516)*	(410)*	(3447)*
	(1637)**	(2852,2960)**	(3244)**	(505,511)**	(406)**	(3452)**
	[0.366]***	[0.95, 0.135]***	[0.00]***	[1.39, 0.97]***	[0.98]***	[0.144]***
(D7)	(1635)*	(2860,2965)*	(3244)*	(485,511)*	-	-
	(1639)**	(2845, 2968)**	(3242)**	(501,510)*	-	-
	[0.24]***	[0. 52 ,0.168]***	[0.061]***	[3.19, 0.19]***		

Where:-
***Theoretical frequency.**
****Experimental frequency.**
*****Error% due to main difference in the experimental measurements and theoretical treatment of vibration spectrum**.

E) Theoretical electronic spectra for the (IP) free ligand and (D1-D7) its metal complexes:

The electronic spectra of the free ligand and its metal complexes have been calculated and the wave numbered for these compounds showed some deviations from the experimental values as shown in Table(7) . These deviations in theoretical calculation are generally acceptable due to couplings between the electronic spectra modes and the approximation that each normal mode of the electronic spectra inter acts independently electronic spectra beam (38, 39). The most diagnostic calculated electronic spectra were chosen for the assignment of the free ligand **(IP)** and their metal complexes **(D1 - D7)** which their respective experimental electronic modes as shown in
Table (3).

All the theoretical electronic spectra of [IP and (D1-D7)] compounds were calculated by using the semi- empirical (PM3) method at Geometry Optimization (0.01K.Cal. mol^{-1}) was used, and the comparison between of the experimental data and theoretical data of the electronic spectra for (IP) free ligand and (D1-D7) their metal complexes showed that the percentage of error was with in the range of (0.15-10.56), as is shown in Table (7).

Table (7)

Comparison between the experimental and theoretical of the electronic spectra for (IP) free ligand and (D1-D7) complexes

Comp. No.	***Bands***	***Assignment***
(IP)	(290)*, (294**, [0.013]*** (338)*, (333)**, [0.015]***	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$
(D1)	(533)*, (560)** [4.82]*** (417)*, (434)**,[3.91]*** (363),(377)**, [3.71]***	$^6A_1g \rightarrow {}^4T_1g(G)$ $^6A_1g \rightarrow {}^4Eg$, $^4A_1g(G)$ $^6A_1g \rightarrow {}^4T_2g(4E)$
(D2)	(518)*,(508)**, [1.96]*** (432)*, (455)**, [5.05]***	$^4T_1g \rightarrow {}^4T_2g(F)$ $^4T_1g \rightarrow {}^4A_2g(F)$ $^4T_1g \rightarrow {}^4T_2g(P)$
(D3)	(886)*, (938)**, [5.54]*** (645)*, (616)** [4.71]*** (412)*, (400)** [3.00]***	$^3A_2g \rightarrow {}^3T_2g(F)$ $^3A_2g \rightarrow {}^3T_1g(F)$ $^3A_2g \rightarrow {}^3T_1g(P)$
(D4)	(821)*, (904)**, [9.18]*** (680)*, (679)**, [0.15]*** (486)*,(495)**, [1.82]*** (361)*,(346)**, [4.34]***	$^2B_1g \rightarrow {}^2A_1g$ $^2B_1g \rightarrow {}^2B_2g$ $^2B_1g \rightarrow {}^2Eg$ (IP) →Cu(C.T)
(D5)	(800)*, (767)**, [4.30]*** (559)*,(625)**,	$^4A_2g \rightarrow {}^2T_2g$, ^2Eg $^4A_2g \rightarrow {}^4T_2g(F)$ $^4A_2g \rightarrow {}^4T_1g(P)$

	[10.56]*** (320)*,(322)**, [0.62]***	
(D6)	(645)*.(620)**, [4.03]*** (560)*,(553)**, [0.26]*** (342)*, (339)**, [0.88]***	${}^6A_1g \rightarrow {}^4T_1g(G)$ ${}^6A_1g \rightarrow {}^4Eg, {}^4A_1g(G)$ ${}^6A_1g \rightarrow {}^4T_2g(G)$
(D7)	(792)*, (851)**, [6.93]*** (607)*, (580)**, [4.66]***	${}^2B_2 \rightarrow {}^2E$ ${}^2B_2 \rightarrow {}^2B_1$

Where:-

***Theoretical transitions band of electronic spectra.**

****Experimental transitions band of electronic spectra.**

*****Error% due to main difference in the experimental measurements and theoretical treatment of electronic spectra.**

F) Bond length measurements for the (IP) its metal complexes:

Calculation of parameters has been optimized bond lengths of the free ligand (IP) and its metal complexes by applying the Semi-empirical (PM3) at Geometry Optimization (0.001 $K.Cal.mol^{-1}$), which to give excellent agreement with the experimental data, as shown in Table (8), Fig (3).

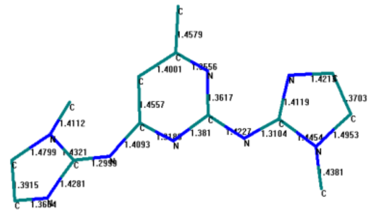
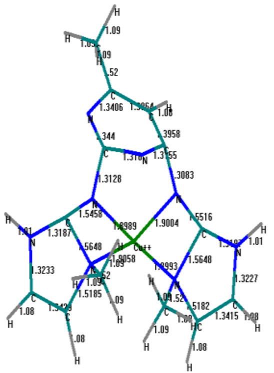
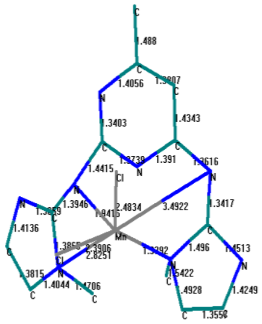
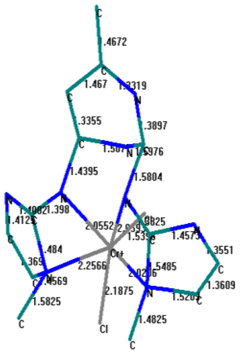
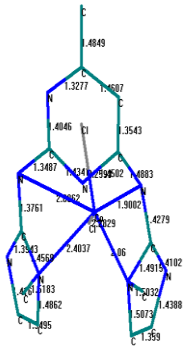
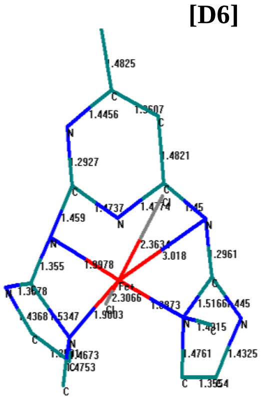
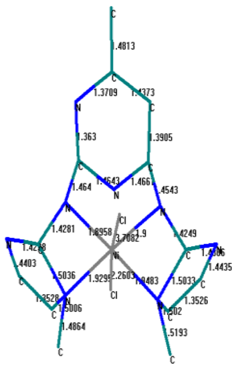
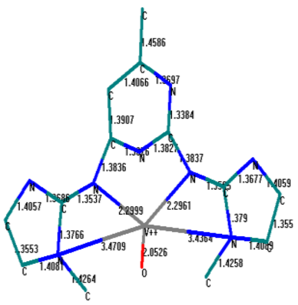
[IP] 	**[D4]** 
[D1] 	**[D5]** 
[D2] 	**[D6]** 
[D3] 	**[D7]** 

Fig (3)
bond lengths (A°) for (IP) ligand and their metal complexes [D1 – D

Table (8)
Selected bond lengths (A°) for (IP) ligand and their metal complexes [D1 – D7]

Comp. No.	***C=N***	***N-CH₃***	***N-H***	***M-Cl***
(IP)	1.359	1.424	0.998	
(D1)	1.367	1.506	0.955	2.437
(D2)	1.401	1.510	0.992	2.2705
(D3)	1.401	1.502	0.992	2.984
(D4)	1.548	1.521	1.01	
(D5)	1.365	1.531	0.988	1.863
(D6)	1.325	1.475	0.992	2.334
(D7)	1.351	1.426	1.04	

Antimicrobial activities of Schiff base and their metal complexes

The **(IP)** ligand and **[D1-D7]**their metal chelates were screened ***in vitro*** in order to evaluate their antibacterial action against*[(Pseudonomous aerugionosa)* as gram negative*]* and*[(Bacillus Subtilis)* as gram positive*]*species as well as antifungal activity against two micro-organism *(Penicillum Spp.)* and *(Aspergillus flavus)* were studied for all compounds ,table (9) at two different concentration. The results from these studies, showed the followings:-

1) All the metal complexes are more toxic as compared with their **(IP)** parent ligand against the same micro-organisms and under the identical experimental conditions, table (9).

2) Some complexes showed a moderate activity, while other exhibited a great enhancement of activity against types of bacteria, Table (9). This difference in synergistic effect between the metal ion and the ligand molecule may be attributed to many factors; of these in that [D5-D7] complexes are considered to be a hard metal ion making their complexes to be less lipophilic, which relatively retard their permeation through the lipid part of the cell membrane. On the other hand the [D1-D4] are considered to be soft metal ions, which render their complexes to be more lipophilic and will facilitate the penetration through the cell wall and affect the environment of cells.

3) The increase in the antibacterial and antifungal activities of metal chelates may be due to the effect of the metal ion on the normal cell process. The toxicity also increases with the increasing concentration of test solution containing the new complexes .These activities may be explained by Tweedy's **Chelation Theory** (40) .

Table (9)

Antibacterial and antifungal activities data for the metal complexes and their parent (IP) ligand

Compo.	*Pseudonomous aeruginosa*		*Bacillus Subtilis*		*Penicillum Spp.*		*Aspergillus flavus*	
	100 ppm	**200 ppm**	**100 ppm**	**200 ppm**	**100 Ppm**	**200 ppm**	**100 ppm**	**200 ppm**
Control (DMSO)	-		-			-		-
(IP)	4	8	-	6	39	30	46	33
[D1]	6	10	6	8	35	22	28	19
[D2]	6	10	8	12	37	24	30	23
[D3]	6	8	8	10	31	15	28	11
[D4]	8	10	6	10	20	10	22	14
[D5]	6	18	6	12	37	18	20	13
[D6]	10	18	8	14	32	20	27	12
[D7]	6	8	8	12	20	10	33	25
Where :[6-8: (+),8-10: (++), >10: (+++)]					**30-40: (+++) , 20-30 :(++++) , 10-20: (+++++)**			

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