Synthesis and characterization of new bidentate chalcone ligand type (NO) and its Mn^{II}, Co^{II}, Ni^{II} and Cu^{II} complexes with study of their antibacterial activity

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Received 28 October 2014 ; Accepted 18 February 2015

Abstract

The aim of the work is synthesis and characterization of new bidentate chalcone ligand type (NO):[(E)-1-(3-aminophenyl)-3-(4-chlorophenyl) prop-2-en-1-one] [H_2L], from the reaction of 3-amino acetophenone with 4-chloro benzaldehyde to produce the ligand [H_2L], the reaction was carried out in ethanol as a solvent under stirring. The prepared ligand [H_2L] was characterized by FT-IR, UV-Vis spectroscopy, ^{1}H, ^{13}C-NMR spectra, Mass spectra, (C.H.N) and melting point. The complexes of ligand [H_2L] were prepared with metal ion M(II).Where M(II) = (Mn ,Co ,Ni and Cu) at reflux ,using ethanol as a solvent and KOH as a base with molecular formula $[M(H_2L)_2]^{+2}$ where: H_2L= ($C_{15}H_{12}NOCl$). All the complexes were characterized by spectroscopic methods (FT-IR, UV-Vis spectroscopy and Atomic Absorbtion) along, chloride content, melting point, molar conductivity and magnetic susceptibility measurements. These measurements showed tetrahedral geometry around (Mn^{II}, Co^{II}, Ni^{II} and Cu^{II}) ions. The biological activity of the ligand [H_2L] and it,s complexes were studied using inhibition method.

Keywords: 3-Aminoacetophenone, 4-Chloro benzaldehyde , Chalcone

Synthesis and characterization of new bidentate chalcone ligand type (NO) and its Mn^{II}, Co^{II}, Ni^{II} and Cu^{II} complexes with study of their antibacterial activity

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تحضير وتشخيص ليكاند جالكون ثنائي السن جديد نوع (NO) ومعقداته لاينوات Mn^{II}, Co^{II}, Ni^{II} and Cu^{II} ودراسة فعاليتها المضادة للبكتريا

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ايمان مطر عطيه
شهد علي صادق

الخلاصة

أن الهدف من العمل تخليق وتشخيص ليكاند جالكون ثنائي السن جديد
[(E)-1-(3-aminophenyl)-3-(4-chlorophenyl) prop-2-en-1-one].[H2L]
من تفاعل 3-aminoacetophenone مع 4-chloro benzaldehyde لينتج الليكاند [H_2L]، أجري التفاعل باستخدام الايثانول كمذيب وبطريقة التحريك الالي، تم تشخيص الليكاند المحضر باستخدام اطياف الاشعة تحت الحمراء واطياف الاشعة فوق البنفسجية وطيف الرنين النووي المغناطيسي لمبروتون ولمكاربون 13 وطيف الكتمة والتحميل الدقيق للعناصر ودرجة الانصهار. حضرت معقدات الليكاند مع الايونات Mn^{II}, Co^{II}, Ni^{II} and Cu^{II} بطريقة التصعيد الحراري باستخدام الايثانول كمذيب، هيدروكسيد البوتاسيوم كقاعدة، بالصيغة $[M(H_2L)_2]^{+2}$ بنسبة مولية (1:2) حيث [H_2L]= $C_{15}H_{12}NOCl$. جميع المعقدات المحضرة شخصت بواسطة الطرائق الطيفية
(اطياف الاشعة تحت الحمراء واطياف الاشعة فوق البنفسجية والامتصاص الذري) فضلاً عن قياس محتوى الكلور، قياسات درجة الانصهار، قياسات التوصيلية المولارية والحساسية المغناطيسية. وتم أقتراح الشكل الهندسي رباعي السطوح حول الايونات الفلزية (Mn^{II} ,Co^{II} ,Ni^{II} and Cu^{II}) . تم دراسة الفعالية المضادة للبكتريا لليكاند [H_2L] ومعقداته باستخدام طريقة التثبيط.

الكلمات المفتاحية: 3-امينو اسيتوفينون ، 4-كلورو بنزلديهايد ، جالكون

Introduction

The chemistry of chalcones generated intensive scientific studies throughout the world, specially interesting for their biological applications. Chalcones are coloured compounds because of the presence of the chromophore and auxochromes[1]. Chalcones are of a great interest because they have aunique structural feature of having a >C=O functional group in conjugation with >C=C < and the whole molecule is in conjugation [2]. The

chalcones are α,β-unsaturated ketones containing the reactive keto ethylene group –CO–CH=CH–. Presence of α,β-unsaturated carbonyl system in chalcone makes it biologically active. Some substituted chalcones and their derivatives have been reported to possess some interested biological properties such as antibacterial, anthelmintic, antifungal, insecticidal, ulcerogenic, anticancer, anti-inflammatory, anaesthetic, analgesic, antileishmanial, antimalarial, antioxidant etc [3].

Chalcones are also key precursore in the synthesis of many biologically important heterocycles such as benzothiazepine[4], 1,4-diketone [5]. Transition metal ions are found in several bacterial species and are reported to play an important role in different enzymatic and physiological reactions, the interaction of chalcones with metal ions may also change the antioxidant properties and also biological effects of the chalcones [6].

Experimental

2.1 Materials and Reagents

All common laboratory chemicals and reagents and their suppliers have been used without further purification. Purity varied from 98% to 99.9%.

2.2 Physical measurements

The following measurements were used to characterize the ligand [H_2L] and it,s complexes. An electro thermal apparatus stuart melting point was used to measure the melting points. FT-IR spectra were recorded by using Shimadzu, (FT-IR)-8300, Infrared Spectrophotometer in the range (4000– 400) cm^{-1}. Spectra were recorded as potassium bromide discs. The electronic spectra of the compounds were obtained using Shimadzu UV-160A- Visible Recording Spectrophotometer, in the range (1100 -200 nm) using quartz cell of (1.0) cm length. The samples with concentration (10^{-3}) mole l^{-1} in DMSO at 25°C were measured.

Electrical conductivity measurements of the complexes were recorded at (25 °C) for (10^{-3}) M solutions of the samples in DMSO as a solvent using Philips pw-Digital Meter Conductivity. Elemental microanalyses were recorded by microanalysis (C.H.N) analyzer, Euro (Vector EA

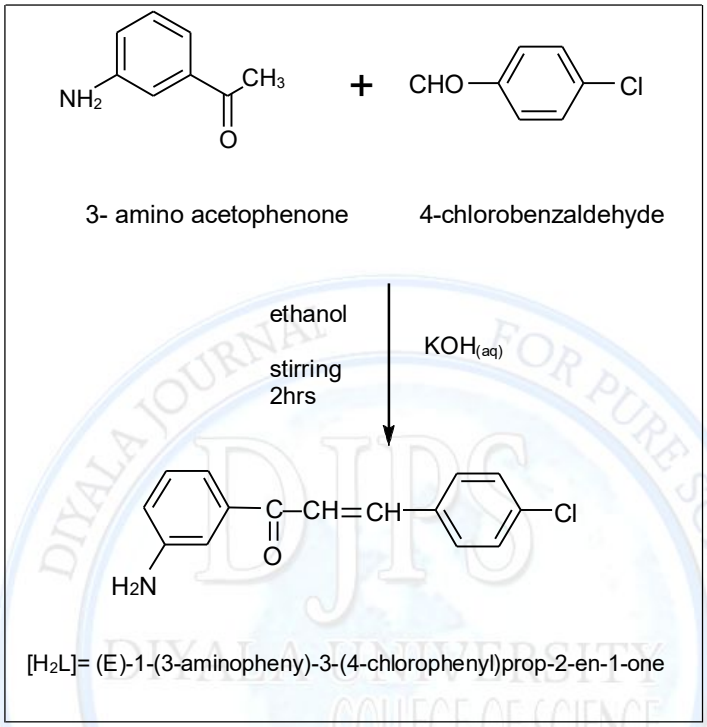
3000A). Spectra for the ligand [H_2L] were recorded in DMSO-d^6 using Brucker, model: Ultra Shield 300 MHz, origin: Switzerland and are reported in ppm (s). The chloride contents for complexes were determined by potentiometric titration method on (686-Titro Processor-665.Dosimat Metrohm Swiss). The metal contents of the complexes were determined by atomic absorption (A.A) technique, using a Shimadzu (A.A 680 GBC 933 plus) atomic absorption spectrophotometer. A known amount of each metal complex was digested with 15ml of concentrated HNO_3 and diluted to a volume of 100ml with deionized water. Then, the metal content in the complexes were determined using atomic absorption spectroscopy. The magnetic susceptibility of the complexes was obtained by using (Balance Johnson Mattey) [7].The mass spectrum for the ligand [H_2L] was obtained by Electron-Impact (EI) on Shimadzu GCMSQPA 1000 spectrometer.

Synthesis

3.1. Synthesis of the ligand [H_2L]

An equimolar mixture of (0.2 gm, 1.47 mmole) 3-aminoacetophenone and (0.2 gm, 1.42 mmole) 4-chlorobenzaldehyde are dissolved in ethanol in 25 ml conical flask. The mixture was stirred with a magnetic stirrer and 10 ml of KOH solution was added dropwise into it. The mixture was stirred at room temperature for 2 hrs. The completion of the reaction (monitored by TLC), the crude mixture was poured in to ice water and then acidified the product with 10% HCl solution. The bright yellow coloured compound is washed with water thoroughly and dried and recrystallised from absolute ethanol to give chalcone as light yellow solids. Weight (0.33), yield (86.8%), m.p (148-150)°C. The synthesis route of the ligand is shown in scheme -1.

Scheme -1: Synthesis route of the ligand [H_2L]



The elemental microanalysis and some physical properties of the ligand [H_2L] were given in table -1.

Table -1: Elemental microanalysis and some physical properties of the ligand [H_2L]

Compound	Empirical formula	M.wt	Yield %	M.P C°	Color	Found (calc.) %		
						C	H	N
[H_2L]	$C_{15}H_{12}ClNO$	257.71	86.8	(148-150)	yellow	68.94 (69.91)	4.59 (4.69)	5.31 (5.43)

M.P=melting point; Calc. =calculated

3.2. Synthesis of the ligand [H_2L] complexes with some metal ions.

Synthesis of $[Mn(H_2L)_2]^{+2}$ complex (1) .

The metal solution of $MnCl_2.4H_2O$ (0.07g, 0.38 mmole) in (10) ml ethanol was stirred for (10) minutes. The ligand solution (0.1 g, 0.38 mmole) in (10) ml ethanol after adjusted to pH=9 using few drops of KOH solution was added to the ligand solution. The resulting mixture was heated under reflux for (2) hrs. Then, the mixture was filtered and the precipitate

was washed with an excess of ethanol and dried at room temperature during (24) hrs. A mustard solid was obtained. Weight (0.15 g), yield (68.18 %), m.p (200-202) °C.

A similar method to that mentioned in preparation of (Mn^{II}) complexes was applied for the preparation of (Co^{II}), (Ni^{II}) and (Cu^{II}) complexes. The physical properties and elemental analysis of complexes is given in table -2 below:

Table -2: Some physical properties of the prepared complexes and its reactants quantities

No.	Empirical formula	Colour	M.P	Wt of metal salt (g)	Wt of product (g)	Yield %	Λ_m $M_S.cm^{-1}$
1	$[Mn(H_2L)_2]^{+2}$	Mustard	202-200	0.07	0.15	68.18	70.8
2	$[Co(H_2L)_2]^{+2}$	Olive	130-128	0.09	0.13	61.90	73.6
3	$[Ni(H_2L)_2]^{+2}$	Green	217-215	0.09	0.15	71.42	78.5
4	$[Cu(H_2L)_2]^{+2}$	Brown	125-123	0.06	0.16	80	71.9

Wt= Weight

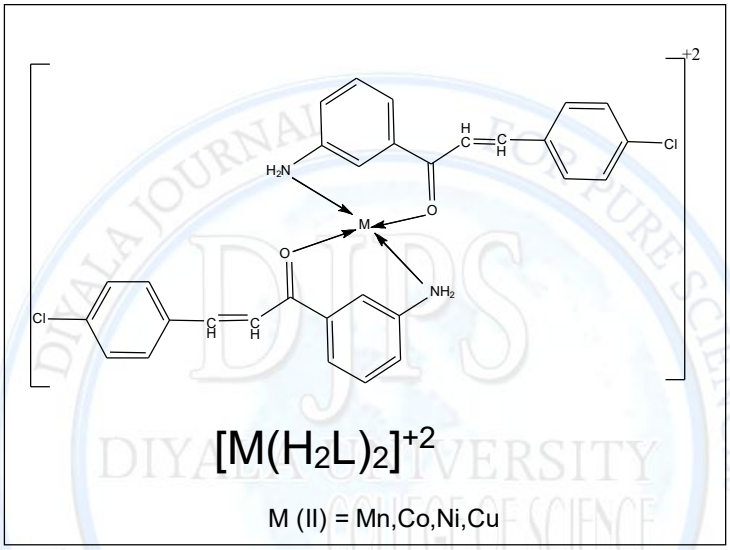
3.3 Biological activity [8, 9]

In vitro bacterial activities of the ligand [H_2L] and it complexes have been carried out against the pathogenic bacteria like *Escherichia coli* and *Bacillus subtilis*, using nutrient ager medium by disc diffusion method. The test solution were prepared in DMSO absolute having the concentration (10^{-3}) mole/liter and soaked in filter paper of (5) mm diameter and (1) mm thickness. These discs were placed on the already seeded plates and incubated at 37 °C for (24) hrs .The diameters of the inhibition zone around each disc were measured after (24) hrs.

Results and Discussion

The elemental analyses showed 1:2 (metal: ligand) stoichiometry for all complexes figure -1.

Figure -1: The proposed structure of the complexes



The analytical data of the ligand and it,s metal complexes corresponded well with the general formula $[M(H_2L)_2]^{+2}$, where M= Mn(II), Co(II), Ni(II) and Cu(II), L= $C_{15}H_{12}ClNO$. The complexes were coloured, stable in air, soluble in DMSO and DMF and insoluble in water and common solvents. The high values of molar conductance for all complexes in DMSO solution refer to electrolytic nature with 1:2 ratio for all metal complexes table -3.

Table -3: Physical properties and analytical data of complexes

No.	Empirical formula	M.wt	Color	M.P (°C)	Found, (Calc)%	
					M	Cl %
1	$[Mn(H_2L)_2]^{+2}$	568.35	Mustard	202-200	9.25 (9.52)	nil
2	$[Co(H_2L)_2]^{+2}$	572.35	Olive	130-128	10.18 (10.26)	nil
3	$[Ni(H_2L)_2]^{+2}$	572.11	Green	217-215	10.63 (10.22)	nil
4	$[Cu(H_2L)_2]^{+2}$	576.96	Brown	127-125	10.53 (10..97)	nil

4.1 Infrared spectra

Important spectral bands for the ligand and it's metal complexes are presented in table -4. The FT-IR spectrum of the ligand show bands at 3464 and 3369 cm^{-1} assignable to $\upsilon_{asy}(NH_2)$ and $\upsilon_{sy}(NH_2)$ stretching vibration, respectively[10]. Other bands at 3057, 1656 and 1604 cm^{-1} assignable to υ(C-H) aromatic, υ(C=O) carbonyl and υ(CH=CH) vinylic stretching vibration, respectively [11-13].

The FT-IR spectra of all metal complexes, show bands in the range (1720-1666) cm^{-1}, assigned to υ(C=O) group [14], which was shifted to higher frequencies in comparison with that of free ligand [H_2L] at (1656) cm^{-1} ,indicating the ligand binds with metal ions through the oxygen of the carbonyl group. Also the spectra show bands in ranges (3452-3421) cm^{-1} and (3358-3346) cm^{-1}, assigned to $\upsilon_{asy}(NH_2)$ and $\upsilon_{sy}(NH_2)$ respectively [15], these bands were shifted to lower frequencies in comparison with that of free ligand [H_2L] at (3464),(3369) cm^{-1} indicating the ligand binds with metal ions through the nitrogen of the amine group. At lower frequency the complexes exhibited new bands around (577-557) cm^{-1} and (495-466) cm^{-1} which are assigned to ν(M-N) and ν(M-O) vibration modes, respectively [16,17].

Table -4: FT-IR spectral data (wave number υ⁻) cm^{-1} of the ligand complexes with some metal ions

Compound	υ_{as} (NH_2) $\upsilon_s(NH_2)$	υ(C=O)	υ(CH=CH)	δ(N-H)	υ(M–N)	υ(M–O)
$[H_2L]$	3464 3369	1656(s)	1604	1622	_	_
$[Mn(H_2L)_2]^{+2}$	3452 3346	1720	1589	1660	569	495
$[Co(H_2L)_2]^{+2}$	3444 3356	1666	1591	1622	567	484
$[Ni(H_2L)_2]^{+2}$	3421 3358	1664	1589	1622	577	486
$[Cu(H_2L)_2]^{+2}$	3448 3348	1664	1608	1622	557	466

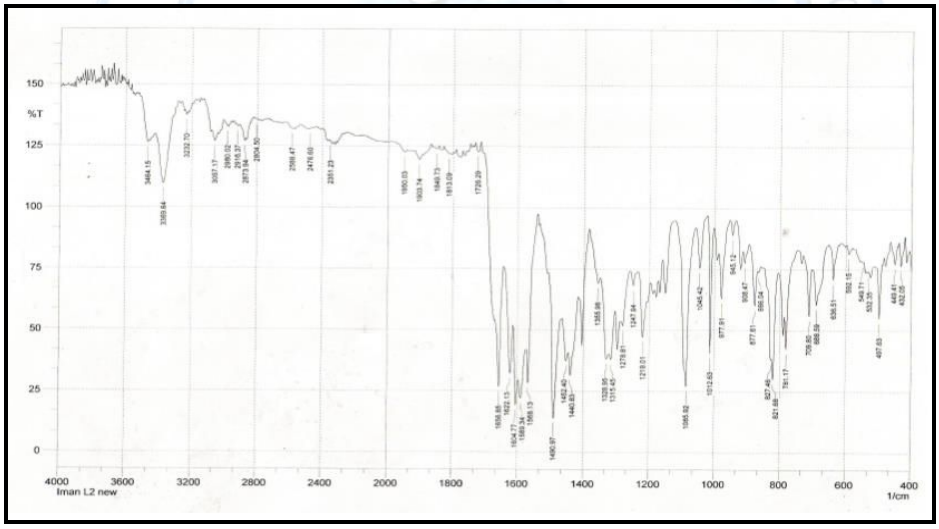


Figure -2: The FT-IR spectrum of ligand chalcone $[H_2L]$

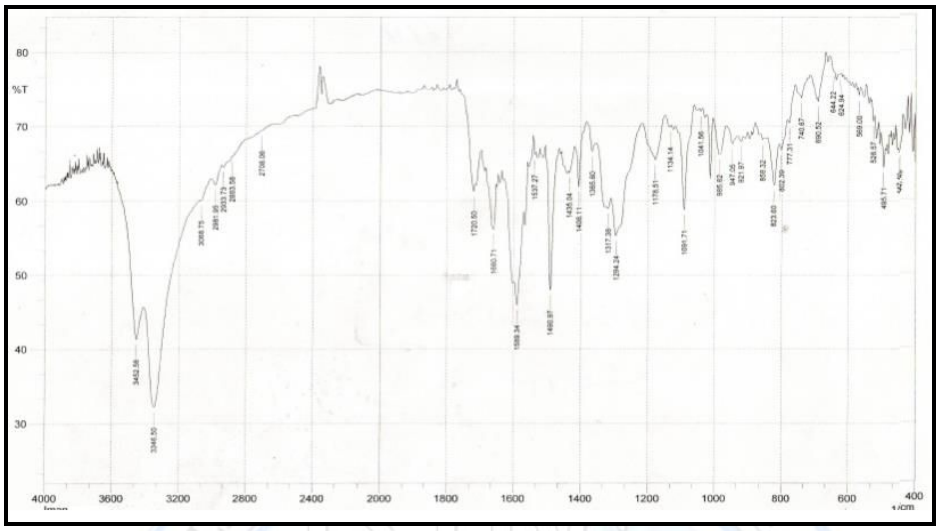


Figure-3: The FT-IR for the $[Mn(H_2L)_2]^{+2}$ complex

4.2 ^{1}H-NMR spectrum of ligand [H_2L]

The ^{1}H-NMR spectrum of the ligand in DMSO with TMS as an internal standard showed a multiplet at 8.50-8.42 ppm for the hydrogens of the aromatic ring, (table -6,figure-4, a singlet at 7.81 and 7.60 ppm for the two hydrogens of CH=CH, a multiplet at 7.15–6. 56 ppm for the four hydrogens of the aromatic ring, a multiplet at 5.32 ppm for the two hydrogen of amine group[18].

Table -6: ^{1}H-NMR data for ligand [H_2L] measured in DMSO-d^6 and chemical shift in ppm (δ)

Compound	Funct. Group	δ (ppm)
[H_2L]	($C_{6''}$, $C_{5''}$, $C_{3''}$, $C_{2''}$)	(8.50-8.42) (4H,m)
	(CH=CH)	(7.81,7.60) (1H,1H,s)
	(C_6, C_5, C_4, C_2)	(7.15-6.56) (4H,m)
	NH_2 (amine group)	(5.32) (2H, m)

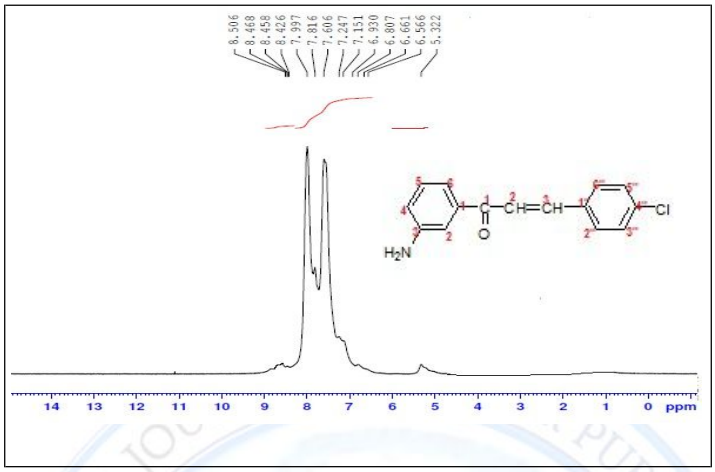


Figure -4: The ^{1}H-NMR for the ligand [H_2L]

4.3 ^{13}C-NMR spectrum of ligand [H_2L]

The ^{13}C-NMR spectrum of the ligand [H^2L] in DMSO-d^6 displayed signals corresponding to the various proton and carbon which confirms the structure of the ligand as shown in table -7:

Table -7: ^{13}C-NMR data for ligand measured in DMSO-d^6 and chemical shift in ppm (δ)

Compound	Functional groups	δ (ppm)
[H_2L]	C=O	189.7
	C_3 for CH=CH group	142.7
	C_2 for CH=CH group	122.7
	$(C_1,C_2, C_3, C_4, C_5, C_6)_{aceto..}$ for aromatic ring	151.4-134.6
	$(C_{1"},C_{2"},C_{3"},C_{4"},C_{5"},C_{6"})_{benza..}$ for aromatic ring	133.6-115.5

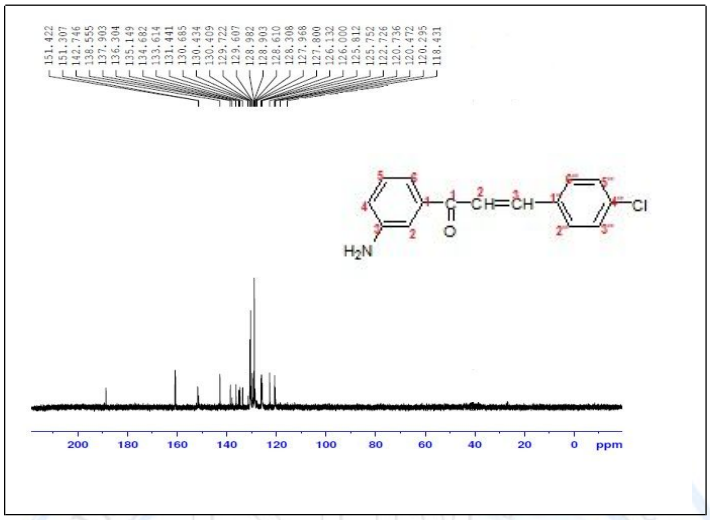


Figure -5: The ^{13}C-NMR for the ligand [H_2L]

4.4 EI-Mass spectrum of ligand [H_2L]

The electrospray (+) mass spectrum of [H_2L], shows the parent ion peak at (M/Z=257), which corresponds to [M^+], other fragments and their relative abundance and fragmentation pattern are shown in figure -6.

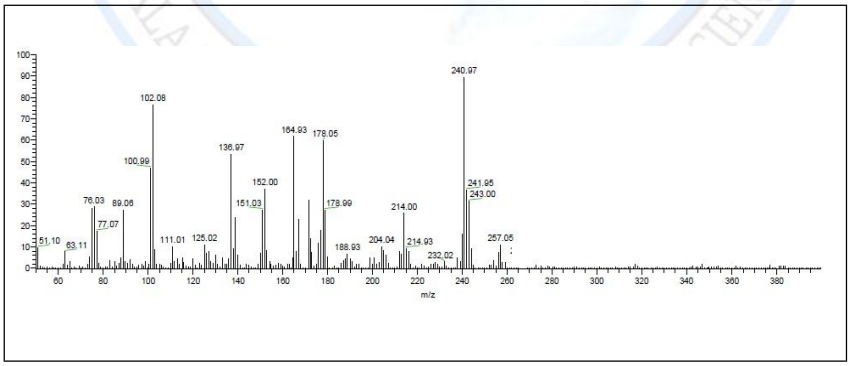


Figure -6: EI-mass spectrum for the ligand [H_2L]

4.5 Electronic spectra, magnetic moments and conductivity measurements

The electronic spectra for ligand [H_2L] and it complexes are shown in table -8, together with the magnetic moment indicate tetrahedral geometry around the metal atoms studied.

Table -8: Electronic spectral data of ligand and it metal complexes

No.	Compound	μ_{eff} (BM)	Wave length nm	Wave number Cm^{-1}	ε_{max} $molar^{-1}$	Assignment
1	[H_2L]	–	280 316	35714 31645	1500 1631	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$
2	$[Mn(H_2L)_2]^{+2}$	5.8	262	38167	1430	L.F
			310	32258	1326	C.T
			908	11013	1	$(^6A_1 \rightarrow {}^4E, {}^4T_1)$
3	$[Co(H_2L)_2]^{+2}$	4.7	260	38461	1510	L.F
			314	31847	1441	C.T
			906	11037	126	$^4A_2 \rightarrow {}^4T_{1(P)}$
4	$[Ni(H_2L)_2]^{+2}$	3.1	264	37878	802	L.F
			310	32258	730	C.T
			908	11013	11	$^3T_1 \rightarrow {}^3T_{1(P)}$
5	$[Cu(H_2L)_2]^{+2}$	2.1	260 312	37593 32051	1316 1356	L.F C.T
			906	11037	4	$^2T_2 \rightarrow {}^2E$

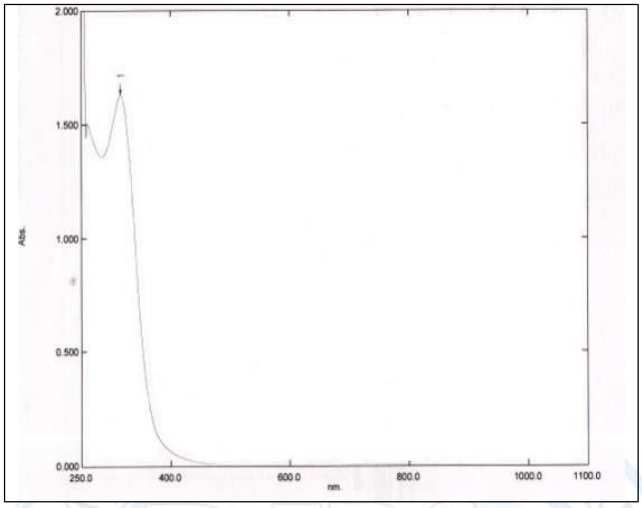


Figure -7: Electronic spectrum of the ligand [H_2L]

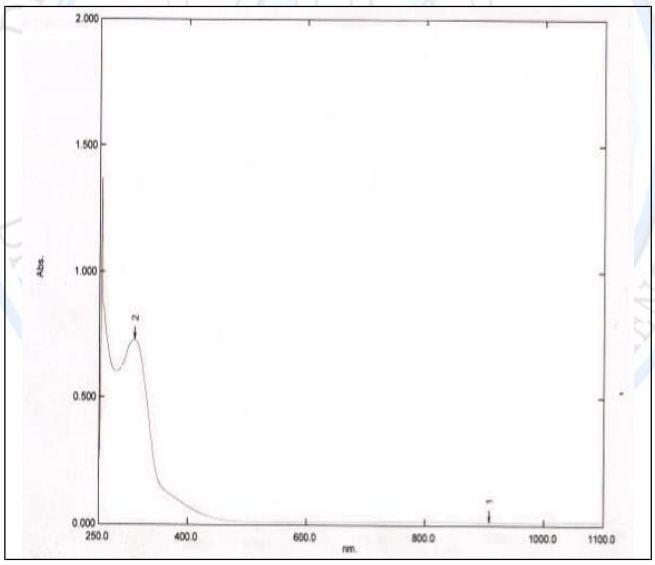


Figure -8: Electronic spectrum of the $[Ni(H_2L)_2]^{+2}$

5- Biological activity

The biological activity of the ligands [H_2L] and it complexes were studied by using inhibition method [19-22] for two types of pathogenic bacteria. Two types of bacteria were gram positive which is *Staphylococcus aureu* and *Escherichia coli*, The compounds show

inhibition diameter against the type of bacterial (*Escherichia coli*) except ligands [H_2L], the results indicate that the complexes show more activity than the ligand [H_2L] under similar experimental conditions, table -9, this may be due to that the chelation considerably reduces the polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible electron delocalization over the whole chelate ring such, chelation could also enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane [23].

Table -9: Inhibition circle diameter in millimeter for the ligands [H_2L] and it,s complexes

No.	Compounds	*Staphylococc usaureu*	*Escherichia coli*
1	[H_2L]	–	16
2	$[Mn(H_2L)_2]^{+2}$	–	24
3	$[Co(H_2L)_2]^{+2}$	–	28
4	$[Ni(H_2L)_2]^{+2}$	–	22
5	$[Cu(H_2L)_2]^{+2}$	–	29
C	DMSO(control)	–	–

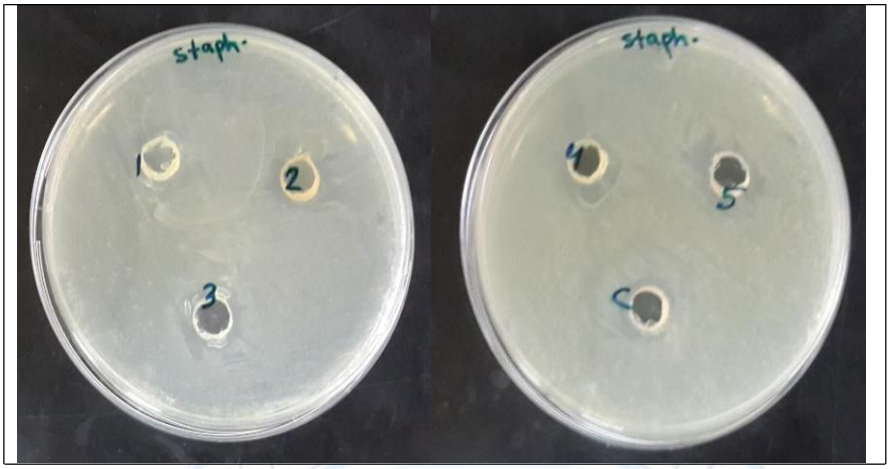


Figure -9: The biological activity (*Staphylococcus aureu*) of the ligand and its complexes

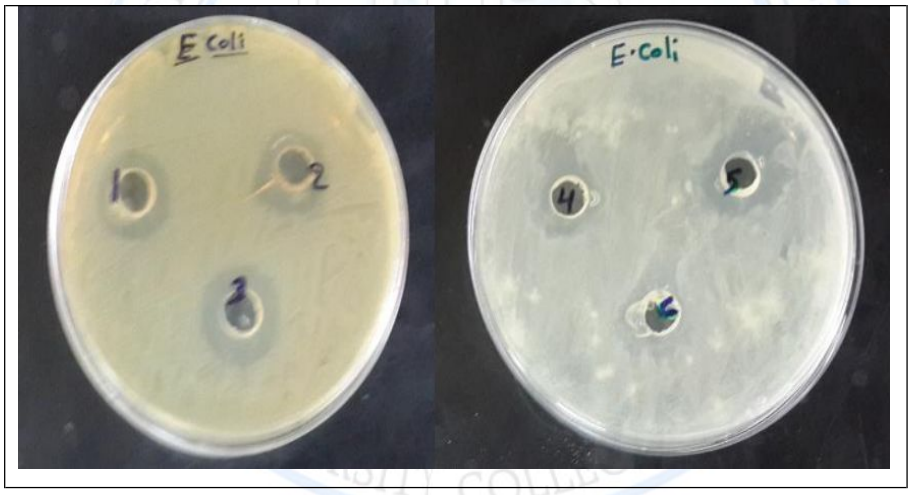


Figure -10: The biological activity (*Escherichia coli*) of the ligand and its complexes

Conclusion

Structure of the synthesized ligand chalcone was confirmed from their respective IR,^{1}H-NMR studies. From the antimicrobial screening it was observed that all the compounds exhibited activity. In this paper we have explored the synthesis and coordination chemistry of some ligand complexes. The mode of bonding and overall structure of the complexes were

determined through physico-chemical and spectroscopic methods. The results show that the solid complexes with a ratio of M: L as (1:2).

References

1. S. H. Shah and P. S. Patel, ***Derpharma Chemica***, 2012, 4(1), 468-472.
2. S. P. Vaijayanthi and N. Mathiyalagan, ***J. Chem. Bio. Phy. Sec. A***, 2012, 2(3), 1281-1286.
3. B. C. Das, G. Mariappan, S. Saha, D. Bhowmik and Chiranjib, ***J.Chem. Pharm. Res***., 2010, 2(1), 113-120.
4. O. Prakash, A. Kumar, A. Sadana, R. Prakash, P.S. Singh, M.R. Claramunt, D. Sanz, I. Alkortac and J. Elguero, ***Trtrahedron***, 2005, 61(27), 6642-6651.
5. S. Raghavan and K. Anuradha, ***Tetrahedron Lett***.,2009,43(29), 5181-5183.
6. S. B. Bukhari, S. Memona, M.M. Tahir and M.I. Bhanger, ***J. Molec. Struc***., 2008, 892,39.
7. D.Nicholls***, "Complexes and First-Row Transition Elements",***translate by Wissam, Ibrahim Aziz, Mousl University press,1984.
8. M.N. Sultana, S. Arayne and M. Afzal, ***Pakistan Journal of Pharmaceutical Sciences,*** 2003,1,59.
9. M.S. Suresh and V. Prakash, ***International Journal of the Physical Sciences,*** 2010,5(14), 2203.
10. H. Rostkowska, M.J. Nowak, L. Lapinski, M. Bertner, T. Kulikowski, A.Les and L. Adamowicz, ***Spectro chim. Acta,*** 1993, 49A, 551.
11. G. Socrates, ***"Infrared Characteristic Group frequencies***", Wiley, New York, 1980.
12. S. Mohan and Dr. K. Prasada Rao, ***International Journal of Pharmaceutical Research and Development,*** 2012, 4(4), 97-101.
13. B. Tiwavi, A. Pratapwar, A. Tapas, S. Butle and B. Vatkar, ***Int. J. Chem. Tech. Res.,***2010, 2(1), 499-503.
14. V. N. Patange and B. R. Arbad, ***J. Serb. Chem. Soc.,*** 2011, 76(9), 1237-1246.
15. R.M. Silverschtien, Bassler and Morril, "***Spectrophotometers Indentification of Organic Compounds"***, Translated by Ali Hussain And Suphi Al-Azawi, 1981.
16. A.S. kindeel, I.J. Dawood and M.R. Aziz, ***J. Baghdad for Sci.,*** 2013, 10(2), 396.

17. M.B. Halli, V.B. Patil, R.B. Sumathi and K. Mallikarjun, ***Dev Pharma Chemica,*** 2012, 4(6), 2360.
18. R. N. Patel and R. V. Patel, ***Euro. J. Exp. Bio.,*** 2012, 2(5), 1492-1496.
19. J.R. Anacona, ***J. Coord. Chem.***, 2006,54, 355– 365.
20. D. Petra, Z. Tatjano and P. Boriset. ***J. inorg. Bio. chemistry***, 2005, 2, 432.
21. S. C. Tauber and R. Nau, "***Immunomodulatory properties of antibiotics***", Current molecular pharmacology, 2008, 1, 68.
22. N. Sultana and M. S. Arayne, ***Pakistan J. pharma. Sci.,*** 2007, 4, 305.
23. H.N. Aliyu, U. Sani and A. Galadima, ***European J. Sci. Res.,*** 2011, 2, 276.