Synthesis, characterization and antimicrobial Studies of complexes of some metal ions with 5(2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole

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Abstract:-

A new series of Fe (III) , Co (II) , Ni (II) and Cu (II) complexes of the Schiff base, 5 (2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole were prepared and characterized .The imine behaves as a bidentate. The nature of bonding and the stereochemistry of the complexes were deduced from metal analyses, infrared, electronic spectra,magnetic susceptibility and conductivity measurements, an octahedral geometry was suggested for all complexes except the copper complex has a square planar geometry .preliminary in vitro tests for antimicrobial activity show that all the prepared compounds except iron complex display good activity to gram positive *Staphelococcus aures* and gram negative *Escherchia coli*.

Key words:- synthesis, thioether, 1, 3, 4- thiadiazole, metal complexes, biological activity.

Introduction:-

Thiadiazole derivatives especially those of 2-thio ether -1, 3, 4-thiadiazole -5- substituted are one class of heterocycles which have attracted a significant interst in medicinal, chemistry and they have a wide range of pharmaceutical and biological activities including antimicrobial, antifungal , inflammatory ,and antihypertensive.[1,2].

Schiff bases of heterocyclic compounds offer a versa file and flexible series of ligands capable to bind with various metal ions to give complexes with suitable properties for theortical /practical applications [3-5]. They are found to be useful in catalysis ,industry and medicine[6-8]. The wide range of applications of the ligand and its' metal complexes aroused our interest to prepare a new series of some metal complexes and study their biological activity.

Instrumentation:-

The metal analyses were carried out on a Shimadzu atomic absorption spectrophotometer, the FTIR spectra in the range (4000-200) cm^{-1} were recorded as CsI discs on a Shimadzu IR Prestige -21 spectrophotometer ,UV-visible spectra in the range (200-1100)nm were recorded using Shimadzu UV-vis.160A.Ultra-violet spectrophotometer. The magnetic susceptibility values of the prepared complexes were obtained at room temperature using magnetic susceptibility Balance of Burker Magnet BM6.Molar conductance of the complexes were measured in DMF as a solvent at room temperature using HANNAEC 214 conductivity type. Melting point were recorded on a hot stage Gallen Kamp melting point apparatus.

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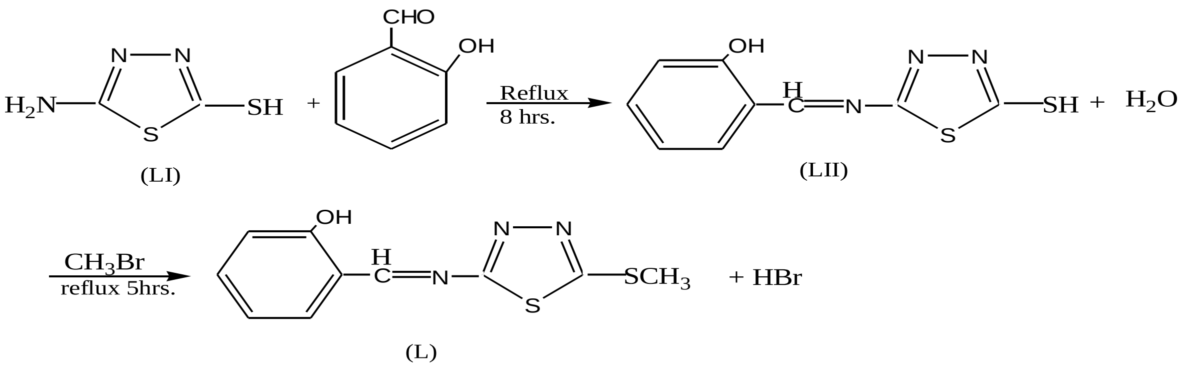
Method and Material:-

Synthesis of 5-(2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole. (L)

The starting material (LI) :-5-Amino 2-mercapto-1,3,4-thiadiazole was prepared according to the literature method [9], while (L) 5-(2-hydroxy benzylidine)-2-marcapto -1,3,4-thiadiazole was prepared according to previous work[10], by mixing (0.5g,0.003mole) of (LI) with (0.003mole,0.366g) of salicaldyhde in absolute ethhanol (15ml) and few drops of glacial acetic acid. The mixture was refluxed for 8 hrs, then cooled to room temperature. Yellow crystals were formed, the product was recrystallized from ethanol and dried under vacuum. The new ligand (L) 5-(2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole was prepared by dissolving (1.0 mole) of the Schiff base (LII) in ethanolic solution with (1.0 mole) of potassium hydroxide solution. The mixture was stirred well and (1.0 mole) of methyl bromide was added and refluxed for 5hrs.The precipitate was separated on cooling and filtered. The product(L) was washed with cold ethanol then dried under vacuum.



Scheme (1): Synthesis of 5-(2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole (L)

Preparation of Complexes:-

The complexes were prepared by the addition of ethanolic solution of the suitable metal salt nickel dichloride hexahydrate,copper dichloride dihydrate, cobalt dinitrate hexhydrate ,and Iron trichlorid nonahydrate to the ethanolic solution of the ligand (L) potassium hydroxiuad (1%) in 1:1 mole ratio for copper and iron complexes and 2:1 for cobalt and nickel complexes. After refluxe for one and half an hour, crystalline colored precipitates formed at room temperature, the resulting solids were filtered off, washed with cold ethanol and dried at 50°C. Table (1) shows the physical properties of these complexes.

Biological activity:-

The antibacterial activity of these compounds was determined by the agar diffusion method [11], using *Staphylococcus auras* (G$^+$) *Escherichia coli* (G$^-$) ,10mM and 5Mm of these compounds was placed on an agar seeded with the test organism. The plates were incubated for 24 hrs at 37 °C. The zone of inhibition formed was measured in mm and represented by (+) ,(++) and (+++) depending upon the diameter and clarity, Table (4).

Results and Discussion:-

A-Chemistry

Physical characteristic ,metal analyses ,magnetic susceptibility and conductivity data of the complexes are given in tables (1and 3).The analytical data of the complexes corresponded to the general formula can be deduced as $[ML_2(H_2O)_2]$.x EtOH ,Where; M =Co , Ni and x=2.5 ,0.5 respectively and $[M_2L_2(H_2O)_n(Cl)_m]$.xH_2O,where ; M = Fe ,Cu;n=2,0;m=4,2 and x=4,1 respectively .All complexes were readily soluble in DMF ,and were found to be stable toward air and moisture ,as well as most of them were decomposed before melting.

The IR spectra of the complexes were compared with that of the free ligand to determine the change that might happened during the complexation. The band at 1627 cm^{-1} is characteristic of the azomethaine nitrogen atom present in the free ligand.The lowering in this frequency region (1620-1615) cm^{-1} observed in all complexes , indicates the involvement of the nitrogen atom of azomethaine in coordination [12,13] . The spectrum of the ligand ,showed a band at 894 cm^{-1} assigned to hydrogen .bonded OH bending vibration [14].This assignment is supported by disappearance of the band when hydrogen of the hydroxyl is replaced by the metal .The phenolic (C-O) stretching vibration ,that appeared at 1285 cm^{-1} in the Schiff base [15,16], underwent to shift toward higher frequencies with splitting in all of the prepared complexes. This shift confirms the participation of oxygen atom in the (C-OM) bond [13, 17]. These observations indicate that this ligand behaves as a bidentate through nitrogen atom of azomethaine and oxygen atom of phenolic moiety. These absorptions were further supported by the appearance of υ_{M-N}, υ_{M-O},and υ_{M-Cl} , frequencies respectively (13). In the present study there is a medium band at 1610, 1608 and1615 cm^{-1} for all complexes except copper on, which may be assigned to the presence of the coordinated water molecule in these complexes [13]. The observed band around (3442-3540)cm^{-1} in the spectra of all complexes assigned to the υ_{-OH} suggested to the presence of ethanol or water molecule in the crystal lattic of the complexes[13,18].

B. Electronic spectra and magnetic moment data of the metal complexes:-

Electronic spectra, and magnetic susceptibility studies were used with the structural to confirm the geometry of the complexes, the electronic spectra of the prepared complexes were recorded for their solution in DMF in the range (200-1100) nm.

The electronic spectra and magnetic moment of the metal complexes are listed in table (3) .Generally, in all spectra of complexes, the absorption bands are due to $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ transitions that observed in the spectrum of the free ligand so the band at 410 nm were shifted to lower frequencies because of the coordination of the ligand with metal ions.

1- **FeL:** Three absorption bands of the brown complex were observed at 660,555 and 392 nm, the former may be due to the spin forbidden transitions $^6A_1g \longrightarrow {}^4T_1g$, $^6A_1g \longrightarrow {}^4T_2g$ and ligand $\longrightarrow$ Fe (CT) [19, 20], which may gain intensity as a result of the vibronic mechanism in octahedral field around ferric ion .The magnetic moment is 5.83 BM with five unpaired electrons indicates an octahedral configuration [19, 21].

2-**CoL:** The μ_{eff} value measured for the Co (II) complex, table (3) is 4.83 BM , indicating octahedral geometry of this brown complex .The spectrum of this complex showed a bands at 652,533 and a shoulder at 475 nm.The former band would be due to a $^4T_1g \longrightarrow {}^4T_2g$, $^4T_1g \longrightarrow {}^4A_2g$ and $^4T_1g \longrightarrow {}^4T_1g_{(P)}$,transitions [21,22] indicating an octahedral configuration around Co(II) ion [19,21].

3-**<u>NiL:</u>** The reflectance spectrum of the mononuclear Ni (II) complex,showed a weak band at 832 nm and another one at 583 nm as well as a shoulder band its at 452nm which could be attributed to the $^3A_2g \longrightarrow {}^3T_2g$, $^3A_2g \longrightarrow {}^3T_1g$ and, $^3A_2g \longrightarrow {}^3T_1g_{(P)}$ transitions respectively [23,24].The magnetic moment of the complex is 3.19BM which agrees well with the know values for nickel (II) complexes in octahedral geometry[19].

4-**<u>CuL:</u>**The spectrum of Cu(II) complex ,showed a broad absorption band at 677 nm which could be attributed to the $^2A_1g \longrightarrow {}^2B_1g$ transition in a square planer geometry[19].The shift of the absorption band to lower energy than the expected for square planer, may be due to the distortion of (Jahn-Taller).This geometry is confirmed by the measured magnetic moment value 1.35 BM ,this result agree with those published in dimeric complexes [19,22].

C. Molar conductance of the metal complexes of the ligand:-

The conductance measurements, recorded for 10^{-3}M solutions of the metal complexes in DMF, are listed in table (3) .All complexes are non-conducting indicating their neutrality and that the cation have replaced the hydroxyl proton of the ligand molecules .According to the above results the following structures are suggested for the metal complexes.

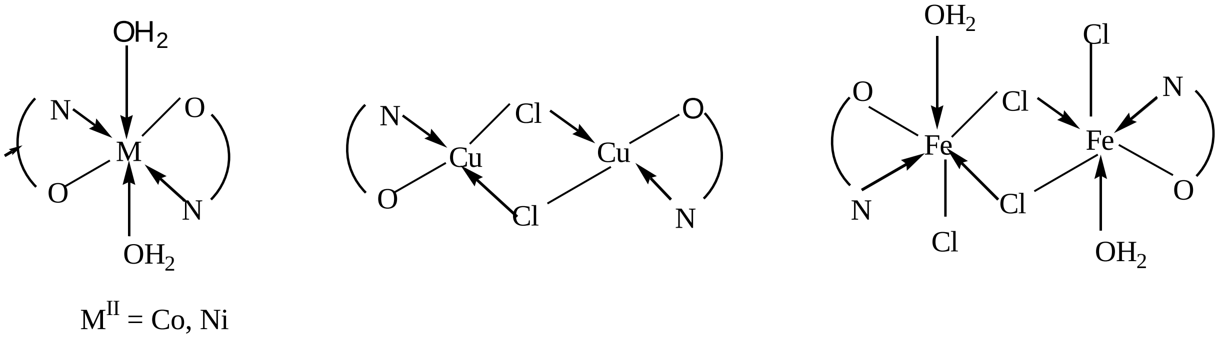


Figure (1): Suggested structures for the metal complexes of the new ligand

B-Biological Activity

The preliminary screening results reveal that the compound contained 5-(2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole complexes exhibited the highest antibacterial activity against *Staphelococcus aures and Echerchia coli* for some metal ions, while others retarded it ,this phenomena is known as synergistic effect [25].The results of the antimicrobial activity are shown in table (4) and figure(2 & 3).

Conclusion:-

The ligand 5-(2-hydroxy benzylidine) -2-thio ether -1, 3, 4-thiadiazole was prepared. The ligand was treated with different metal ions salt to affored the corresponding through oxygen atom of hydroxyl group and nitrogen atom of azomethaine, leading to the formation of member ring chelate as square planer geometry proposed for the copper complex.The other complexes were proposed to be octahedral geometries. Biological activity data showed that the reported compounds have a significant antimicrobial activity against *Staphelococcus aures* and *Echerchia coli* except iron complex.

Table (1): Physical data for the ligand and its' metal complexes

Compound	Colour	Melting Point °C	Yield%	Metal content Found(Cal.)	Suggested Formula Structure
L	Pale yellow	218-220	70	—	$C_{10}H_9N_3OS_2$
FeL	Brown	280*	48	12.06 (12.86)	$[Fe_2L_2(H_2O)_2Cl_4].4H_2O$
CoL	Brown	176-178	55	7.68 (8.00	$[CoL_2(H_2O)_2].2\frac{1}{2}$ EtOH
NiL	Green	242*	72	9.02 (9.516)	$[NiL_2(H_2O)_2].\ \frac{1}{2}$ EtOH
CuL	Brown	170-172	42	17.70 (17.68)	$[Cu_2L_2Cl_2].H_2O$

*Decomposition point.

Table (2): Characteristic IR bands (cm^{-1}) of the ligand and its' metal complexes

Compound	$\upsilon_{C=N}$	υ_{C-O}	υ_{NCS}	υ_{CSC}	υ_{M-N}	υ_{M-O}	υ_{M-Cl}	υ_{-OH}
L	1627.9	1285	1068 1070	660	---	---	---	3470
FeL	1615	1292 1275	1072 1070	663	488	520	383	3450 $1610_{coordinate}$ H_2O
CoL	1620	1292 1273	1068 1070	660	483	514	---	3540 $1608_{coordinate}$ H_2O
NiL	1620	1292 1275	1068 1066	665	488	516	---	3540 $1615_{coordinate}$ H_2O
CuL	1618	1290 1273	1073 1070	660	420	520	375	3442

Table (3): Magnetic moment, spectral data (cm^{-1}) and conductance measurement of the ligand and its' metal complexes

Compound	μ_{eff} BM	Bands cm^{-1}	assignment	EC* (μScm^{-1})
L	------	$2.43 *10^4$ $3.03 *10^4$ $3.5 *10^4$	$n\rightarrow\pi^*$ $\pi\rightarrow\pi^*$ $\pi\rightarrow\pi^*$	-----
FeL	5.83	$1.51 * 10^4$ $1.8 * 10^4$ $2.55 * 10^4$	${}^6A_1g \longrightarrow {}^4T_1g$ ${}^6A_1g \longrightarrow {}^4T_2g$ $L \longrightarrow Fe$ (CT)	35.10
CoL	4.83	$1.53 * 10^4$ $1.87* 10^4$ $2.1* 10^4$	${}^4T_1g \longrightarrow {}^4T_2g$ ${}^4T_1g \longrightarrow {}^4A_2g$ ${}^4T_1g \longrightarrow {}^4T_2g_{(P)}$	30.01
NiL	3.19	$1.2* 10^4$ $1.71* 10^4$ $2.21* 10^4$	${}^3A_2g \longrightarrow {}^3T_2g$ ${}^3A_2g \longrightarrow {}^3T_1g$ ${}^3A_2g \longrightarrow {}^3T_1g_{(P)}$	15.21
CuL	1.35	$1.47* 10^4$	${}^2A_1g \longrightarrow {}^2B_1 g$	21.86

EC*: Electrical conductance, 10^{-3}M solution in DMF.
CT: Charge transfer

Table (4): Antimicrobial activity of the Schiff base and it's metal complexes

Comp.	*Staphelococcus aures*		*Echerchia coli*	
	10 µm	5 µm	10 µm	5 µm
L	-	-	-	-
FeL	-	-	-	-
CoL	+++	++	++	++
NiL	++	++	++	++
CuL	++	++	++	+

(-) : Inactive(inhibition zone < 5mm).
(+): Slightly active (inhibition zone 5-10mm).
(++): moderately activity (inhibition zone 11-20mm).
(+++): high activity (inhibition zone >20mm).

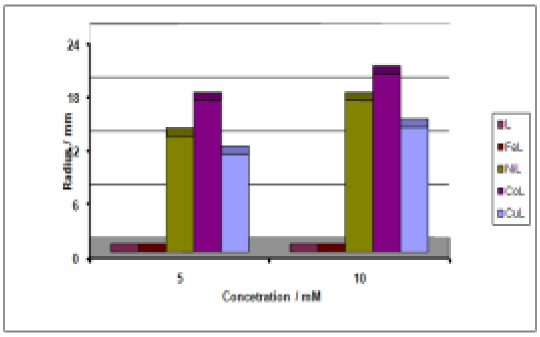


Figure (2): Effect of the ligand and its complexes toward *E.coli* bacteria

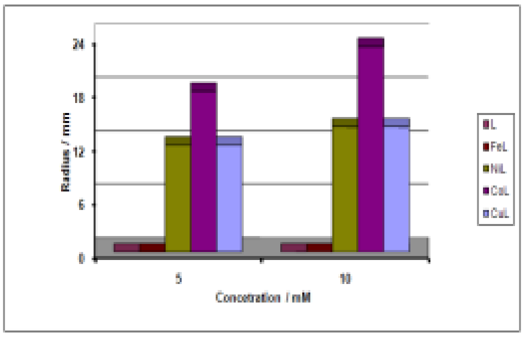


Figure (3): Effect of the ligand and its complexes toward *S.aures*

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تحضير وتشخيص ودراسة الفعالية البايولوجية لبعض معقدات 5(2-هايدروكسي بنزايلدين) -2-ثايو ايثر -1و3و4- ثايادايازول

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الخلاصة:

تم تحضير سلسلة من معقدات الحديد (III) والكوبلت (II) والنيكل (II) والنحاس (II) مع قاعدة شف الجديدة
5(2- Hydroxy benzylidine)-2- thio ether -1,3,4- thiodizole
تم تشخيص المعقدات المحضرة باستخدام تقنية الامتصاص الذري لطيف الاشعة تحت الحمراء والاشعة فوق البنفسجية والحساسية المغناطيسية بالاضافة الى قياسات التوصيلية الكهربائية وتبيت ان الليكاند ثنائي السن واقترح الشكل الهندسي ثماني السطوح لجميع المعقدات المحضرة ماعدا النحاس ذو الشكل الشكل المربع المستوي. تم التقييم الحيوي لهذه المركبات ضد نوعين من البكتريا staphelococcus aures و Escherchia coli وبتركيزين حيث اظهرت التاثير التازري للفعالية فيما عدا معقد الحديد .