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 benzylidene) -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 Staphylococcus aureus and gram negative Escherchia coli.

Key words:- synthesis, thioether, 1, 3, 4- thiazole, 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 interest 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 theoretical /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 Csl 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 benzylidene) -2-thio ether -1, 3, 4-thiadiazole, (L)
The starting material (LI) -5-Amino 2-mercaptop-1,3,4-thiadiazole was prepared according to the literature method [9], while (L) 5-(2-hydroxy benzylidene)-2-mercaptop -1,3,4-thiadiazole was prepared according to previous work[10], by mixing (0.5g,0.003 mole) of (LI) with (0.003 mole, 0.366g) of salicylaldehyde in absolute ethanol (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 benzylidene) -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.

\[
\begin{align*}
\text{H}_2\text{N}-\text{S}-\text{H} & \quad \rightarrow \quad \text{CHO} \\
\text{N} & \quad \text{CH} \\
\text{NH} & \quad \text{N} \\
\text{OH} & \quad \text{OH} \\
\text{SH} & \quad \text{H}_2\text{O} \\
\end{align*}
\]

Scheme (1): Synthesis of 5-(2-hydroxy benzylidene) -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 hydrate, cobalt nitrate hexahydrate, and Iron trichlorid nonahydrate to the ethanolic solution of the ligand (L) potassium hydroxiod (1%) in 1:1 mole ratio for copper and iron complexes and 2:1 for cobalt and nickel complexes. After reflux 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 aureus (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 [ML₂(H₂O)ₓ] x EtOH, Where; M = Co, Ni and x = 2.5, 0.5 respectively and [ML₂(H₂O)ₓ(Cl)ₓ] x H₂O, where; M = Fe , Cu, Mn = 2.0, n = 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 azomethane 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 azomethane 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 shift toward higher frequencies with splitting in all of the prepared complexes. This shift confirms the participation of oxygen atom in the (C−O−M) bond [13, 17]. These observations indicate that this ligand behaves as a bidentate through nitrogen atom of azomethane and oxygen atom of phenolic moiety. These absorptions were further supported by the appearance of ν(N=N), ν(N=O), and ν(C=O) frequencies respectively (13). In the present study there is a medium band at 1610, 1608 and 1615 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 ν(OH) suggested to the presence of ethanol or water molecule in the crystal lattice 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 π−π* and n−π* 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. FeL₄: 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 ²A₁g ——— ²T₁g, ²A₁g ——— ²T₁g and ligand ——— 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. CoL₄: The μₑₑ 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 ²T₁g ——— ²T₁g , ²T₁g ——— ²A₂g and ²T₁g ——— ²T₁g (p) , transitions [21, 22] indicating an octahedral configuration around Co(II) ion [19, 21].
3-NiL₂: The reflectance spectrum of the mononuclear Ni (II) complex, showed a weak band at 382 nm and another one at 583 nm as well as a shoulder band at 452 nm which could be attributed to the $^3\text{A}_2g \rightarrow ^1\text{T}_2g$, $^3\text{A}_2g \rightarrow ^3\text{T}_{1g}$ and $^3\text{A}_2g \rightarrow ^3\text{T}_{1g(p)}$ transitions respectively [23,24]. The magnetic moment of the complex is 3.19 BM which agrees well with the known values for nickel (II) complexes in octahedral geometry [19].

4-CuL₂: The spectrum of Cu(II) complex showed a broad absorption band at 677 nm which could be attributed to the $^3\text{A}_2g \rightarrow ^1\text{B}_3g$ transition in a square planar 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-Teller). This geometry is confirmed by the measured magnetic moment value 1.35 BM. This result agrees with those published in dimeric complexes [19,22].

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

The conductance measurements, recorded for 10⁻⁷ 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 has replaced the hydroxyl proton of the ligand molecules. According to the above results the following structures are suggested for the metal complexes.

![Structures](image)

$\text{M}^1 = \text{Ni, Co, Ni}$

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 benzylidene) -2-thiobenzaldehyde -1, 3, 4-thiadiazole complexes exhibited the highest antibacterial activity against Staphylococcus aureus 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 benzylidene) -2-thio benzaldehyde -1, 3, 4-thiadiazole was prepared. The ligand was treated with different metal ions salt to afford 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 Staphylococcus aureus and Echerchia coli except iron complex.
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Table (1): Physical data for the ligand and its metal complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Colour</th>
<th>Melting Point °C</th>
<th>Yield(%)</th>
<th>Metal content Found(CuL)</th>
<th>Suggested Formula Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>Pale yellow</td>
<td>218-220</td>
<td>70</td>
<td></td>
<td>Cu₃L₃N₃(OH)₃</td>
</tr>
<tr>
<td>FeL</td>
<td>Brown</td>
<td>290°</td>
<td>48</td>
<td>12.06 (12.86)</td>
<td>[Fe(3L)(H₂O)₃Cl₂]·4H₂O</td>
</tr>
<tr>
<td>CoL</td>
<td>Brown</td>
<td>176-178</td>
<td>55</td>
<td>7.08 (8.00)</td>
<td>[Co(3L)(H₂O)₃]·2½H₂O</td>
</tr>
<tr>
<td>NiL</td>
<td>Green</td>
<td>242°</td>
<td>72</td>
<td>9.02 (9.516)</td>
<td>[Ni(3L)(H₂O)₃]·2½H₂O</td>
</tr>
<tr>
<td>CuL</td>
<td>Brown</td>
<td>170-172</td>
<td>42</td>
<td>17.70 (17.68)</td>
<td>[Cu(3L)(Cl)₂]·H₂O</td>
</tr>
</tbody>
</table>

*Decomposition point.

Table (2): Characteristic IR bands (cm⁻¹) of the ligand and its metal complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>w₁(νC=O)</th>
<th>w₂(νC≡N)</th>
<th>w₃(νC-N)</th>
<th>w₄(νC₉-H)</th>
<th>w₅(νC₉-H)</th>
<th>w₆(νC₉-H)</th>
<th>w₇(νC₉-H)</th>
<th>w₈(νC₉-H)</th>
<th>w₉(νC₉-H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>1627.9</td>
<td>1285</td>
<td>1068</td>
<td>1070</td>
<td>660</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>3470</td>
</tr>
<tr>
<td>FeL</td>
<td>1615</td>
<td>1292</td>
<td>1072</td>
<td>1070</td>
<td>663</td>
<td>488</td>
<td>520</td>
<td>383</td>
<td>3450</td>
</tr>
<tr>
<td>CoL</td>
<td>1620</td>
<td>1292</td>
<td>1068</td>
<td>1070</td>
<td>660</td>
<td>483</td>
<td>514</td>
<td>---</td>
<td>3540</td>
</tr>
<tr>
<td>NiL</td>
<td>1620</td>
<td>1292</td>
<td>1068</td>
<td>1066</td>
<td>665</td>
<td>488</td>
<td>516</td>
<td>---</td>
<td>3540</td>
</tr>
<tr>
<td>CuL</td>
<td>1618</td>
<td>1290</td>
<td>1073</td>
<td>1070</td>
<td>660</td>
<td>420</td>
<td>520</td>
<td>378</td>
<td>3442</td>
</tr>
</tbody>
</table>

Table (3): Magnetic moment, spectral data (cm⁻¹) and conductance measurement of the ligand and its metal complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bₚ,(μₘ)</th>
<th>Bands cm⁻¹</th>
<th>assignment</th>
<th>EC (μS cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>5.83</td>
<td>2.43 *10⁴</td>
<td>π→π⁺</td>
<td>----</td>
</tr>
<tr>
<td>FeL</td>
<td>1.51 *10⁴</td>
<td>3.03 *10⁴</td>
<td>π→π⁺</td>
<td>35.10</td>
</tr>
<tr>
<td>CoL</td>
<td>1.21 *10⁴</td>
<td>1.87 *10⁴</td>
<td>π→π⁺</td>
<td>30.01</td>
</tr>
<tr>
<td>NiL</td>
<td>1.71 *10⁴</td>
<td>2.21 *10⁴</td>
<td>π→π⁺</td>
<td>15.21</td>
</tr>
<tr>
<td>CuL</td>
<td>1.37 *10⁴</td>
<td>1.47 *10⁴</td>
<td>π→π⁺</td>
<td>21.86</td>
</tr>
</tbody>
</table>

EC': Electrical conductance, 10⁻⁴ M solution in DMF.
CT: Charge transfer

Table (4): Antimicrobial activity of the Schiff base and its metal complexes

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Staphylococcus aureus</th>
<th>Echerchia coli</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 μm</td>
<td>5 μm</td>
</tr>
<tr>
<td>L</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FeL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CoL</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>NiL</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>CuL</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

(-): Inactive (inhibition zone < 5mm).
(;++): Slightly active (inhibition zone 5-10mm).
(;++): Moderately active (inhibition zone 11-20mm).
(;+++): High activity (inhibition zone >20mm).
References:

1. Polshettiwar, V. and Varma, R. 2008. Greener and rapid a cccs to bio-active heterocycles: one-pot solvent-free synthesis of 1,3,4-oxadiazoles and 1,3,4-thiadiazole, Tetrahedron Letters, 49(5), 879-883.


تحضير وتشخيص ودراسة الفعالية البيولوجية لبعض معقدات (2-هيدروكسي بنزآلدين) -2-ثايرو أنثر -1- و 3-ثاياديازول

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قسم الكيمياء كلية العلوم بجامعة بغداد
**قسم الاقتصاد الزراعي كلية التربية للبنات جامعة بغداد

الخلاصة:
تم تحضير سلسلة من معقدات الحديد (III) والكوليك (I) والثيوكولي (II) والثيوكولي (II) مع قاعدة شف الحديد (2-Hydroxy benzylidine )-2-thio ether -1,3,4-thiodizole

تم تشخيص المعقدات المحضرة باستخدام تقنية الأشعة النقطية للفيضان تحت الماء والأشعة فوق البنفسجية والحساسية المغناطيسية بالإضافة إلى قياسات التوصيلية الكهربائية وتبين ان الليكينيد ثنائي السن واقترح الشكل الهندسي لمعقدات الحديد لجميع المعقدات المحضرة ساعدنا في التصنيف نمو الشكل الشكل المربع Escherchia و staphelococcus aures المستو. تم تقديم الحيوي لهذه المركبات ضد نوعين من البكتيريا coli و تركزين حيث اظهرت النتائج النتائج ألعاب فاعلية فيما عدا معقد الحديد.