Synthesis, characterization and biological studies of some transition metal complexes of hydrazone Schiff base ligand derived from of 2-quinolone and 1-phthalazine hydrazine hydrochloride

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ABSTRACT

Mononuclear solid complexes of transitions metals Mn(II), Fe(III), Co(III), Ni(II), Cu(II) and Zn(II) were synthesized by using Schiff base hydrazone derived from 1-ethyl-4-hydroxy-2(1H)-quinolone and 1-phthalazine hydrazine hydrochloride. The ligand and complexes have been characterized by elemental analysis, UV-visible spectroscopy, FTIR, H1 NMR, mass spectroscopy, magnetic susceptibility, conductivity and X-ray diffraction study. From analytical data the stoichiometry of the complexes has been found to be 1:2 (metal : ligand). The physicochemical study supports the octahedral geometry of all the complexes except Cu(II) having distorted octahedral geometry. The X-ray diffraction data suggests triclinic crystal system for all the metal complexes. The ligand functions as ONN tridentate preferred in the coordination producing octahedral complexes. The antimicrobial studies show the enhancement in the activity of ligand after complexation.

INTRODUCTION

Hydrazones and their metal complexes are having great pharmacological applications as anti-fungal [1], anti-inflammatory [2], anti-bacterial, anti-cancer, anti-tumor agents [3]. Also, the metal complexes of hydrazones have number of applications in molecular sensor [4], anti-oxidative, luminescence probes [5]. The importance of 1-phthalazinehydrazone arises from incorporating 2-quinolone ring with phthalazine ring since quinolone ring is having potential activity. The study of interaction between quinolone and metals is an active area of research in bioinorganic chemistry [6]. Quinolone compounds have interesting biological properties such as antimicrobial [7], anticoccidal [8], antitumor activity. L. D. Popov and his co-workers reported a synthesis and quantum chemical studies of Cu(II), oxovanadium(II) with bis-1-phthalazine hydrazone complexes[9]. Phthalazine hydrazine hydrazone complexes act as potential hypertensive agent. In continuation of our research work on Schiff bases and their metal complexes synthesis [10-11] in the present paper reports the preparation and characterization of some new complexes formed by the reaction of Mn(II), Fe(III), Co(III), Cu(II), Ni(II), Zn(II) with a Schiff base hydrazone ligand that is (E)-1-ethyl-4-hydroxy-3-[1-phthalalazinylhydrazono]-1(H)-quinoline -2-one. The structure of these complexes has been proposed on the basis of physicochemical and spectral analysis. The antibacterial and antifungal activities of the ligand and metal complexes were also investigated against four bacteria and four fungi. A search through literature reveals that no work has been done on the present ligand and its metal complexes.

MATERIALS AND METHODS

All chemicals were of AR grade, purchased from Sigma Aldrich and used for synthesis of ligand. AR grade metal acetates of Co(II), Mn(II) and metal nitrates of Cu(II),Ni(II),Zn(II) from S. D. Fine chemicals were used for complex preparation. Spectral grade solvents were used for spectral measurements. The carbon, hydrogen, nitrogen contents were determined on Thermo Scientific (Flash 2000) CHN elemental analyzer. IR spectra were recorded on
FTIR spectrophotometer model RZXC Perkin Elmer in the range 400-4000 cm\(^{-1}\). The UV/ Vis spectra were recorded on Shimadzu UV 1800 Spectrophotometer for complexes in DMSO. \(^1\)H-NMR spectra of ligand measured in DMSO using TMS as an internal standard. The LC- MS spectra were recorded on a Waters, Q-TOF Micro Mass (LC-MS). Magnetic moments were measured by Guoy's method and were corrected for diamagnetism of the components using Pascal's constants. Conductance were measured on Elico CM-180 Conductometer using \(10^{-3}\) M solution in DMSO. Powder XRD studies were carried out with a Bruker AXS D8 Advance X-ray diffractometer.

**Synthesis of ligand:**
A hot 50ml ethanol was taken in clean and dry round bottomed flask. To this, (0.05 mol 9.82g) 1-phthalazinyl hydrazine hydrochloride was taken. To neutralize the salt of 1-phthalazin hydrazine hydrochloride, strong base, triethyl amine was added. The solution was warmed up to dissolution. In this hot solution, (0.05 mol 11.55g) of 3-acetyl-1-ethyl-4-hydroxy-2(1H)-one was added and the solution was warmed with continuous stirring. Yellow solid product formed was filtered off, washed with ethanol and dried in vacuo. The product was recrystallized from DMF-Ethanol mixture (yield 85% mp.240˚c)

Formation of the Schiff base ligand represented by following reaction.

![Formation of the investigated Schiff base ligand and its proposed structure.](image)

On the basis of elemental analysis, IR, \(^1\)H-NMR and mass spectra the above structure have been proposed for the synthesized ligand

**Synthesis of metal complexes:**
20 mL of a hot methanolic solution of metal salt (0.001mol) was added to (0.002 mol) ligand dissolved in same volume of methanol with constant stirring. After addition of metal salt in ligand solution, 1-phthalazine hydrazone immediately dissolved. The solution was adjusted to pH 7.5-8.5 by adding 10% alcoholic ammonia. This reaction mixture was warmed and stirred on magnetic stirrer for 5 hours. The solid metal complex separates out. It was then filtered, washed with methanol and dried in vacuo.

**RESULTS AND DISCUSSION**

All complexes are coloured solids, stable for air and heat. The complexes are insoluble in water, ethanol, methanol, DCM but easily soluble in polar solvents DMF/DMSO.

The analytical data like colour, melting point, % of elements, the magnetic moments and conductance are presented in Table 1. The elemental analysis and mass spectra of complex show 1:2 (Metal : Ligand) stoichiometry for all the complexes.

**Molar conductance and Magnetic susceptibility measurements:**
Molar Conductance measurements were performed in DMSO (\(10^{-3}\)M) solutions at room temperature. The molar conductance data indicates that all the complexes are non electrolytic in nature.

Magnetic susceptibility of the powdered complexes was carried out by using Guoy's balance method at room temperature with Hg[Co(SCN)4] as a calibrant. The effective magnetic moment values were calculated by using formula,

\[ \mu_{\text{eff}} = 2.83 \left( \chi_{M} T \right)^{1/2} \text{BM} \]

where, \(\chi_{M}\) = molar susceptibility, \(T\) = absolute temperature. The \(\mu_{\text{eff}}\) of metal ions were calculated by applying diamagnetic corrections using Pasca's constants.
The Mn(II) complex has a magnetic moment 5.66 BM in agreement with octahedral geometry. The Fe(III) complex shows magnetic moment 5.9 BM in agreement with reported value of octahedral Fe(III) complex. Co(III) complexes was obtained due to air oxidation [12] which show diamagnetic character which indicates that the Co(III) complex has low spin octahedral geometry [13-14]. The Cu(II) complex shows magnetic moment 2.1 BM higher than spin only value 1.73 of BM due to John Teller distortion. It confirms distorted octahedral geometry. Ni(II) and Zn(II) complexes show diamagnetic character indicating octahedral geometry.

IR spectra:
The FTIR spectrum of metal complexes was compared with that of free ligand in order to investigate the mode of chelation of metal ions with ligand. The IR peaks of free ligand showed some characteristic bands at 3430, 3262, 1634, 1595, 1553, 990 and 751 cm\(^{-1}\) due to NH, OH, CH, C=O(quinolone), >C=N(phthalazine), N-N(stretching) and NH (out of plane) respectively. It is observed that the band attributed to OH in the ligand is also present in all complexes indicates that OH group is not taking part in coordination. The IR stretching frequency of >C=O(quinolone), >C=N, >C=N(phthalazine) shift to lower frequency range which indicates that they form coordinate bond with metal atom. The IR stretching frequency of >C=O(quinolone) shifts to lower frequency 32-49 cm\(^{-1}\) indicates participation of 2-quinolone carbonyl in the metal complexes. The downfield shift in frequency of azomethine nitrogen by 35-62 cm\(^{-1}\) in all the complexes indicates participation of azomethine nitrogen. A downfield shift of >C=N phthalazine ring nitrogen by 3-47 cm\(^{-1}\) in complexes indicates participation of phthalazine ring nitrogen in which was further confirmed by observation of the red shift in 990 cm\(^{-1}\) for N-N stretching frequency [18]. The band appeared at 751 cm\(^{-1}\) due to NH(out of plane) also shifts to higher frequency by 4-8 cm\(^{-1}\) indicating participation of azomethine nitrogen in complexation. The IR spectra of metal complexes show new band in the 571-690 cm\(^{-1}\) region, which can be assigned to \(\nu\) (M-O) and \(\nu\) (M-N) vibrations respectively [19]. The ligand acts as neutral ONN tridentate Schiff base.

UV-visible spectra:
The electronic spectral data of the ligand and its metal complexes were carried out in DMSO. The UV-visible spectra of the synthesized complexes exhibits a low energy absorption. The electronic spectra of Mn(II) complex exhibits band at 18214 cm\(^{-1}\) assigned to the \(^5\text{Alg} \rightarrow ^3\text{T1g}\) d-d transition. The Fe(III) complex show transition at 17513 cm\(^{-1}\) due to T\(_2\)g \(\rightarrow\) A\(_2\)g d-d transition suggest octahedral geometry around the Fe(III) complex [21]. Cu(II) complex showed band at 25974 cm\(^{-1}\) assigned to the charge transfer. The Mn(II), Fe(III), Cu(II) complexes are paramagnetic having octahedral geometry around the metal atom. The complexes of Co(III), Ni(II), Zn(II) does not show prominent transitions in visible region. Broad bands observed at 22371, 22624, 25000 cm\(^{-1}\) in the spectrum of Co(III), Ni(II), Zn(II) complexes respectively are assigned to the LMCT transitions and spectral features of octahedral geometry. The type of d-d transitions can not be identified due to the charge transfer band tailing from UV region to the visible region. In general, the colour of all the complexes is dominated by the charge transfer. Extra
band expected for d-d transitions have been submerged. Co(III) complex, which is diamagnetic indicating low spin octahedral geometry[12]. Ni(II) and Zn(II) complexes are also diamagnetic expected for d^8 and d^10 octahedral systems.

Mass Spectra of the Ligand and its Complexes: In the mass spectrum, the molecular ion peak of the ligand is observed at m/z 374.2(M+1), m/z 375.2(M+2) which confirms the molecular weight of ligand as m/z 373 which is exactly equal to that calculated theoretically from the proposed structure. The molecular ion peaks of the Mn(II), Fe(III), Co(III), Ni(II) complexes are observed at 798.92, 800.1, 805, 803 m/z, respectively corresponding to their molecular masses. This is further supported by the results of elemental analysis. The mass spectra of complexes indicate that there is a formation of 1:2 metal-ligand stoichiometry. The absence of water molecules observed since the molecular ion peaks of complexes exactly match with the mass of 1:2 metal ligand proportion.

Mass spectrum of [Co(III)C_{42}H_{34}N_{10}O_{4}] complex.

1H NMR spectra:
1H NMR spectra of ligand was recorded in DMSO. It shows signals at 1.26 ppm (t,3H,N-CH$_2$-CH$_3$), 2.8 ppm (s,3H,N=C-CH$_3$), 4.26 ppm (q,2H,N-CH$_2$-CH$_3$), 7.1-8.3 ppm (m,8H,H arom), 12.09 ppm (s,1H,N-H), 17.35 ppm (s,1H,-OH enolic) in agreement with the proposed ligand structure.

X-ray diffraction study:
The X-ray diffractogram of representative metals i.e. Mn(II), Fe(II), Co(II) and Ni(II) were scanned in the range 0-60˚ at wavelength 1.54 Å. The X-ray diffraction pattern of the complex with respect to major peaks having relative intensity greater than 10% have been indexed by using computer program[22]. The above indexing program gives hkl planes , unit cell parameters and volume. The diffractogram and associated data gives 20 values for each peak, relative intensity and inter planer spacing (d-values). The diffractogram of Mn(II) complex shows nine reflections with maximum at 20 = (8.612) corresponding to d value 10.2594 Å and cell volume = 1546.5 Å$^3$. The unit cell of Mn(II) complex yields values of lattice constants , a=21.30 Å, b=9.0, c=8.512Å and angle α=88˚, β=108˚, γ=86.5˚. Mn(II) complex exhibit the condition a≠b≠c and α≠β≠γ =90˚ which indicate that Mn(II) complex is of triclinic lattice type. The diffractogram of Fe(III) complex shows fifteen reflections with maxima at 20 = (9.285˚) corresponding to d value 9.517Å. The unit cell of Fe(III) complex yields values of lattice parameters as a = 19.85, b = 8.75, c = 8.9 Å and α =90.8 Å, β =108.012 Å, γ =86.5 and unit cell volume V =1467.2 Å$^3$. In occurrence with these cell parameters of Fe(III) complex, the condition a≠b≠c and α≠β≠γ =90˚ indicate that the complex is of triclinic lattice type. The diffractogram of Co(III) complex shows thirteen reflections with maxima at 20 (9.119) corresponding to d value 9.6895 Å and cell volume = 1491.29 Å$^3$. Observed values for lattice constants a=20.25 Å, b=8.9, c=8.75 Å and α=94˚, β =108.75˚, γ =91˚. Co (III) satisfies the condition a≠b≠c and α≠β≠γ =90˚ which confirms triclinic lattice type. The diffractogram of Co(III) complex shows thirteen reflections with maxima at 20 (9.119) corresponding to d value 9.6895 Å and cell volume = 1491.29 Å$^3$. Observed values for lattice constants a=20.25 Å, b=8.9, c=8.75 Å and α=94˚, β =108.75˚, γ =91˚. Co (III) satisfies the condition a≠b≠c and α≠β≠γ =90˚ which confirms triclinic lattice type. The diffractogram of Ni(II) complex shows eleven reflection with maxima at 20 (11.057) corresponding to d value 7.995 Å, and V=1157.7 Å$^3$. The observed value of lattice constants, a=16.65, b=8.76, c=8.8 and α =94˚, β =109.125˚, γ =84˚ satisfies the condition a≠b≠c and α≠β≠γ =90˚ indicating triclinic lattice type. Overall X-ray studies indicates that all the complexes are of triclinic lattice t X-ray diffractogram of Fe(III) complex.
Antimicrobial activity of the complexes:

The antibacterial activity of the ligand and its complexes were tested against the standard microbial strains, *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus* and *Bacillus subtilis* by agar cup method at fixed concentration of 1%[18] and compared with known antibiotic viz penicillin (Table 2). For fungicidal activity, compounds were screened in vitro against *Aspergillus niger*, *Penicillium chrysogenum*, *fusarium moniliforme*, *Aspergillus flavus* by poison plate method with potato dextrose agar media. The complexes were tested at 1% concentration in DMSO and compared with control (Table 3).

The hydrazone Schiff base and all its complexes individually shows varying degrees of inhibiting effects on the growth of the tested bacterial species. Ligand and the metal complexes do not show activity against Gram-negative bacteria *Escherichia coli*, *Salmonella typhi*. The ligand and some of the complexes show activity against Gram-positive bacteria *Staphylococcus aureus*, *Bacillus subtilis*. The metal complexes show better activity for *Bacillus subtilis*. Only Mn(II), Fe(III) and Ni(II) complexes are found to be active against *Staphylococcus aureus* bacterium. However the activity of these complexes is considerably less than that of standard drug. Results of antifungal testing indicate that the ligand do not have activity against any of the fungi used in present study. Similarly in case of the Fe(II), Cu(II) and Zn complexes antifungal activity is absent. However, the other metal complexes show moderate to high antifungal activity. In these cases it found that the chelates exhibits higher toxicity as compared to their parent ligand.

Table 2 : Report for Antibacterial Testing.

<table>
<thead>
<tr>
<th>Test compound</th>
<th>Inhibition Zone (nm)</th>
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<tbody>
<tr>
<td></td>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td>penicillin</td>
<td>14 mm</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Mn]} )</td>
<td>---</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Fe]} )</td>
<td>---</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Co]} )</td>
<td>---</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Ni]} )</td>
<td>---</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Zn]} )</td>
<td>---</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Cu]} )</td>
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</table>

Legend - ve = No Antibacterial Activity Zone of inhibition = ....... mm

Table 3 : Report for Antifungal Testing

<table>
<thead>
<tr>
<th>Test compound</th>
<th>Aspergillus niger</th>
<th>Penicillium chrysogenum</th>
<th>Fusarium moniliforme</th>
<th>Aspergillus flavus</th>
</tr>
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<tbody>
<tr>
<td>Griseoflin</td>
<td>-ve</td>
<td>-ve</td>
<td>-ve</td>
<td>-ve</td>
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<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Mn]} )</td>
<td>+ve</td>
<td>-ve</td>
<td>+ve</td>
<td>+ve</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Fe]} )</td>
<td>+ve</td>
<td>+ve</td>
<td>-ve</td>
<td>+ve</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Co]} )</td>
<td>RG</td>
<td>RG</td>
<td>RG</td>
<td>RG</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Ni]} )</td>
<td>RG</td>
<td>RG</td>
<td>RG</td>
<td>RG</td>
</tr>
<tr>
<td>( \text{[C}_2\text{H}_2\text{N}_2\text{O}_2\text{Zn]} )</td>
<td>+ve</td>
<td>+ve</td>
<td>-ve</td>
<td>+ve</td>
</tr>
</tbody>
</table>
We have synthesized Mn(II), Fe(III), Co(III), Cu(II), Ni(II), Zn(II) complexes using phthalazinehydrazone formed by condensation of 1-phthalazine hydrazine hydrochloride and 1-ethyl-4-hydroxy-2(1H)-quinolone. The ligand behaves as tridentate with ONN donor sequence in E isomeric form towards the metal ions. The complexes were characterized by analytical and physicochemical measurements, which leads to proposal of octahedral geometry to all the metal complexes except Cu(II) complex having distorted octahedral geometry. The ligand and its complexes were screened for their antibacterial activity against Gram-positive and Gram-positive bacteria. A comparative study indicates that the metal complexes exhibit higher activity against Gram-negative bacteria than the free ligand, but it is weak as compared to standard drug. The ligand and complexes were also tested for antifungal activity. Ligand does not show antifungal activity but the complexes of Mn(II), Co(III) and Ni(II) show antifungal activity against all the tested fungi with reduced growth.

REFERENCES