

## Structural Diversity of 3d Complexes of an Isatinic Quinolyl Hydrazone

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### Abstract

The reaction of the isatinic quinolyl hydrazone ( $H_2L$ ) with Fe(III), Co(II), Ni(II), Cu(II) and VO(II) ions in presence of LiOH afforded mononuclear as well as dimeric chelates. Due to the presence of LiOH, the ligand used its lactim form in all complexes and showed a variety of modes of bonding viz.  $(NNO)^{-}$ ,  $(NO)^{-}$  with or without O- bridging per each metal ion. The mode of bonding and basicity of the ligand depend mainly on the type of the metal ion. The obtained Co(II), Ni(II) and Cu(II)- complexes have the square planar geometry, whereas, Fe(III) and VO(II)- complexes have the octahedral geometry. LiOH behaves as a coligand in case of Fe(III)- complex whereas, it behaves as a deprotonating agent in case of the rest of complexes. The investigated complexes exhibited low to moderate activities against *S. aureus* bacteria. For clarifying their proposed structures, the complexes were subjected to elemental analysis and spectral studies.

**Key words:** Isatinic quinolyl hydrazone complexes, lactim bridging, magnetic properties, antimicrobial activity.

### Introduction

The importance of the quinoline ring arises from its presence in a group of potent alkaloids e.g. quinine and cyanine dyes<sup>1</sup>. Quinoline ring has therapeutic and biological activities<sup>2</sup>. Also, quinolyl hydrazones have anticancer and anti-inflammatory activities<sup>3-5</sup>. Quinolyl hydrazones are known to function as chelating agents and have versatile modes of bonding<sup>6-8</sup>. Recently, the physiological and biological activities of quinolyl hydrazones arise from their tendency to form metal chelates with transition metal ions<sup>3-5</sup>. On the other hand, isatin (1H-indole-2,3-dione) and its derivatives exhibit a wide range of biological activities<sup>3,4</sup>. The indole ring occurs in Jasmine flowers and Orange blossoms<sup>1</sup>. The incorporation of the quinoline ring with the indole ring may enhance the biological activity of such class of compounds. In continuation of our interest on the complexation of quinolyl hydrazones<sup>6-8</sup>, this study is planned to check the role of LiOH on the isolated transition metal complexes (Fe(III), Co(II), Ni(II), Cu(II) and VO(II)) of an isatinic quinolyl hydrazone ( $H_2L$ ); 3-[2-(4-methyl quinolin-2-yl)hydrazono]indolin-2-one<sup>7</sup>; Scheme 1.

### Material and Methods

**Experimental Instrumentation:** Microanalyses were carried out on a Perkin- Elmer 2400 CHN elemental analyzer. Analyses of metal ions followed dissolution of the solid complex in hot concentrated nitric acid,  $HNO_3$ , then diluting with doubly distilled water and filtration. The resultant solution was neutralized with ammonia and the metal ions were then titrated against EDTA. Electronic spectra were recorded on a Jasco V-550 UV/VIS spectrophotometer. IR spectra were recorded on a Bruker Vector 22 spectrometer using KBr pellets. ESR spectra were recorded on a Bruker Elexsys, E 500 operated at X-band frequency. Mass spectra were recorded at 70 eV on a gas chromatographic GCMSQP 1000-EX Shimadzu mass

spectrometer. <sup>1</sup>H NMR spectra were recorded as DMSO- $d_6$  solutions on a Varian Mercury VX-300 NMR spectrometer using TMS as a reference. Molar conductivity was measured as DMF solutions on the Corning conductivity meter NY 14831 model 441. Magnetic susceptibility of the complexes was measured at room temperature using a Johnson Matthey, MKI magnetic susceptibility balance. Melting points were determined using a Stuart melting point apparatus.

The chemicals used in this investigation were of the highest purity available (Merck, BDH, Aldrich and Fluka). They included  $FeCl_3 \cdot 6H_2O$ ,  $CoCl_2 \cdot 6H_2O$ ,  $NiCl_2 \cdot 6H_2O$ ,  $CuCl_2 \cdot 2H_2O$ ,  $VOSO_4 \cdot H_2O$ ,  $LiOH \cdot H_2O$ , aniline, ethyl acetoacetate, phosphorus oxychloride, isatin and hydrazine hydrate (100%). The solvents used in this study were reagent grade and used without further purification.

**Preparation of the Isatinic Hydrazone ( $H_2L$ ):** The ligand was prepared according to our previous publication<sup>7</sup>; an ethanolic mixture of 2-hydrazinyl-4-methyl quinoline (0.01mol) and isatin (0.012 mol) was refluxed for 15 min. The formed scarlet red compound was filtered off, washed with ethanol and crystallized from DMF; Yield: 77% and m.p 302°C.

**Preparation of the Metal Complexes:** A methanolic solution of the metal salt was added gradually to a methanolic solution of the ligand;  $H_2L$ , then, a methanolic solution of lithium hydroxide was added to the reaction mixture in the mole ratio 1 : 1 : 1 ;  $M^{+n} : H_2L : LiOH$ . The reaction mixture was refluxed for 2-4 h to ensure the complete precipitation of the formed complexes. The precipitated solid complexes (1-5) were filtered off, washed several times with methanol to remove any excess of the unreacted starting materials. Finally, the complexes were washed with ether and dried in vacuum desiccators over anhydrous  $CaCl_2$ . All the isolated complexes are

stable at room temperature, non hygroscopic and insoluble in water, partially soluble in alcohols and completely soluble in DMSO and DMF. The molar conductance of millimolar DMF solutions indicates a non-electrolytic nature for all complexes.

**Antimicrobial Activity:** The standardized disc- agar diffusion method<sup>9</sup> was followed to determine the activity of the synthesized compounds against the sensitive organisms *Staphylococcus aureus* (ATCC 25923) as Gram-positive bacteria and *Pseudomonas phaseolicola* (GSPB 2828) as Gram- negative bacteria. The antibiotics chloramphenicol and Cephalothin were used as standard reference in case of Gram- negative and Gram- positive bacteria, respectively. The tested compounds were dissolved in dimethyl formamide (DMF) which have no inhibition activity to get concentration of 2 mg / mL. The test was performed on medium potato dextrose agar (PDA) which contain infusion of 200 g potatoes, 6 g dextrose and 15 g agar<sup>9</sup>. Uniform size filter paper disks (3 disks per compound) were impregnated by equal volume (10  $\mu$ L) from the specific concentration of dissolved tested compounds and carefully placed on inoculated agar surface. After incubation for 36 h at 27 °C, inhibition of the organisms which evidenced by clear zone surround each disk was measured and used to calculate mean of inhibition zones.

## Results and Discussion

**Characterization of the Hydrazone:** The results of elemental analysis of the investigated hydrazone ( $H_2L$ ; scheme 1) are in good agreement with the proposed molecular formula;  $C_{18}H_{14}N_4O$  (302.36): Calcd.: C, 71.50; H, 4.68; N, 18.53 Found: C, 71.40; H, 4.50; N, 18.60. The IR spectrum showed very strong bands at 3333, 1684 and 1633  $cm^{-1}$  assignable to  $\nu(NH)$ ,  $\nu(C=O)$  and  $\nu(C=N)$ , respectively, confirming the lactam nature of  $H_2L$ . Also, the  $^1H$  NMR spectral data of the ligand in  $d_6$ -DMSO relative to TMS provide a further support of the lactam nature of the hydrazone. The mass spectrum of the ligand showed the  $M^+$  peak at  $m/z = 302$  and the base peak at  $m/z = 273$  confirming its formula weight<sup>7</sup>.

**Characterization of the Isatinic Complexes:** In a previous study<sup>7</sup>, the isatinic hydrazone ( $H_2L$ ) was allowed to react with iron(III), cobalt(II), nickel(II) and copper(II) chlorides, as well as oxovanadium(IV) sulfate monohydrate at the mole ratio; 1:1 (scheme 2). However, in an attempt to investigate the role of LiOH on the isolated complexes (the present study), the ligand ( $H_2L$ ) was allowed to react with the same metal ions in presence of LiOH at the mole ratio; 1:1:1. These reactions afforded dimeric and mononuclear complexes (table 1 and scheme 3). In case of complexes 2-4, a base catalyzed dimerization occurs. However, in case of complex 1, a hydroxo complex is obtained in which LiOH acts as a coligand. In contrast, for complex 5, LiOH acts as a deprotonating agent and a mononuclear complex is formed (scheme 3). The proposed structures of the complexes are in good harmony with the

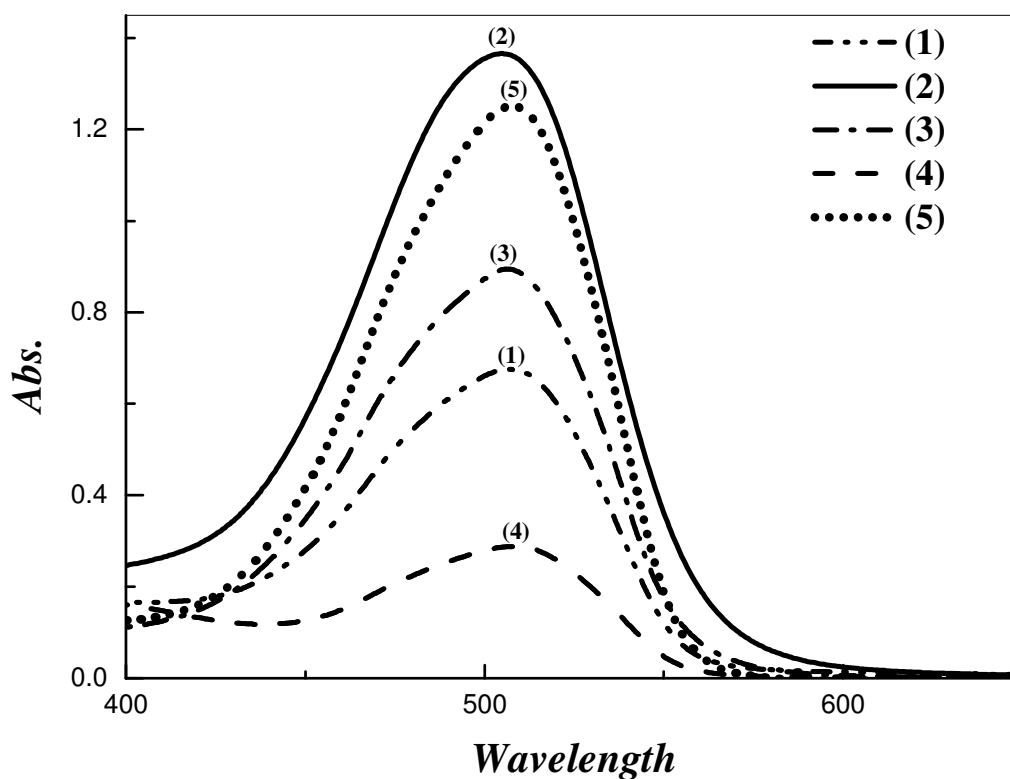
results of the elemental analyses (table 1). The isatinic hydrazone showed a variety of modes of bonding towards the different metal ions *viz.* mono basic NO bidentate using its lactim form without O- bridging (complexes 1,5) or with O- bridging (complexes 3,4). In case of complex 2, the hydrazone behaves as a dibasic NNO tridentate with O-bridging. However, the latter mode of bonding is not observed in our previous study for a similar isatinic hydrazone; 3-[2-(4,8-dimethylquinolin-2-yl) hydrazono] indolin-2-one<sup>8</sup>. This is due to the presence of the Me-group in the 8- position in close proximity to the heterocyclic N- atom of the quinoline ring i.e. increasing the steric hindrance at the heterocyclic N- atom of the quinoline ring suppresses its participation in the chelation<sup>8</sup>. The dimeric complexes (2-4) have the *trans* arrangement and are formed *via* lactim bridging. Characterization of the obtained complexes was achieved *via* elemental analyses, magnetic and conductivity measurements as well as spectral studies.

**IR Spectra of the Complexes:** Most complexes showed a broad band in the range 3436-3386  $cm^{-1}$  due to  $\nu(OH)$  of the associated water or methanol molecules. The band at 1633  $cm^{-1}$  assignable to  $\nu(C=N)$  in the free ligand was shifted to higher or lower values indicating its participation in the chelation with  $\pi$ - electron delocalization<sup>10</sup>. In all complexes, the band located at 1684  $cm^{-1}$  due to  $\nu(C=O)$  of the free ligand disappeared indicating the participation of the lactim form in the chelation. For complex (2), the variable intensity bands of the quinoline ring of the free hydrazone at 1554,1482 and 1455  $cm^{-1}$  are greatly altered indicating the participation of the heterocyclic N- atom of the quinoline ring in the complexation<sup>11</sup>.

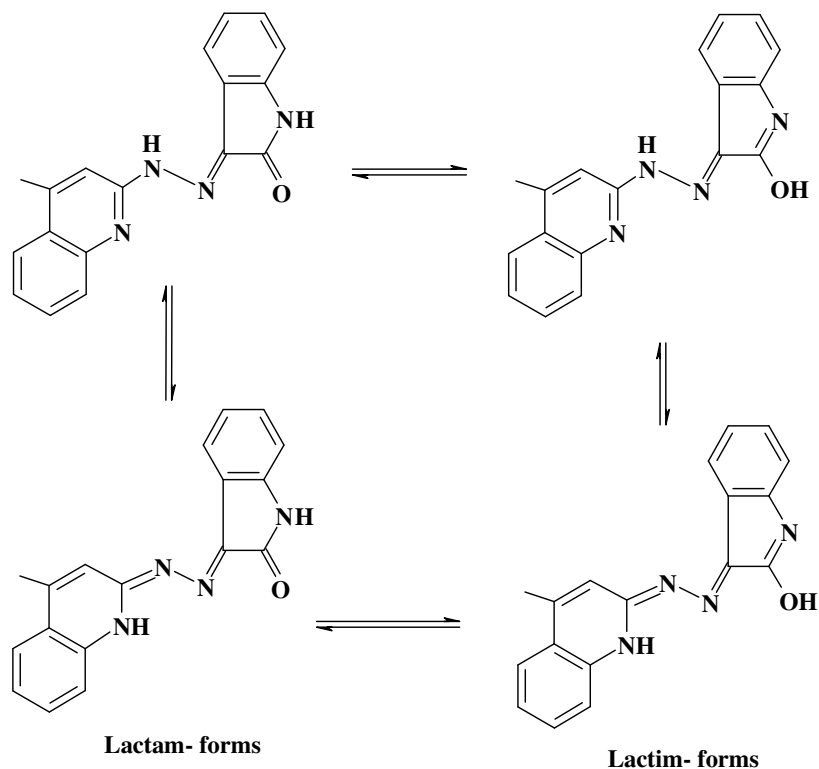
**Magneto Chemistry:** The magnetic properties of the complexes provide valuable information for distinguishing their stereochemistry. Room temperature magnetic moment data showed that the effective magnetic moment ( $\mu_{eff}$ ) of the iron(III)- complex (1) has the value 5.97 B.M. (table 1) which is consistent with five unpaired electrons suggesting an  $sp^3d^2$  hybridization, and falls within the range reported for high spin  $O_h$ - geometry<sup>12</sup>. The copper(II)- complex (4),  $3d^9$ -system and oxovanadium (IV) complex (5);  $3d^1$ -system exhibit  $\mu_{eff}$  values of 1.59 and 1.86 B.M. (table 1) indicating the presence of one unpaired electron. In addition, the cobalt(II)-complex (2);  $3d^7$ -system showed an effective magnetic moment of 1.66 B.M. confirming its square planar geometry which is related also to one unpaired electron. This value confirms its dimeric nature ( $\mu_{eff} < 1.73$  B.M.; spin only value in absence of a ligand field)<sup>7</sup>. Also, the diamagnetism of the nickel(II)-complex (3);  $3d^8$ - system supports its square planar geometry. In general, square planar complexes rather than tetrahedral complexes usually arise from strong field ligands (ligands tending to cause spin pairing), the stronger the ligand, the more favored is the *trans* isomer (scheme 3).

**Table-1**  
**Analytical and physical data of the isatinic complexes**

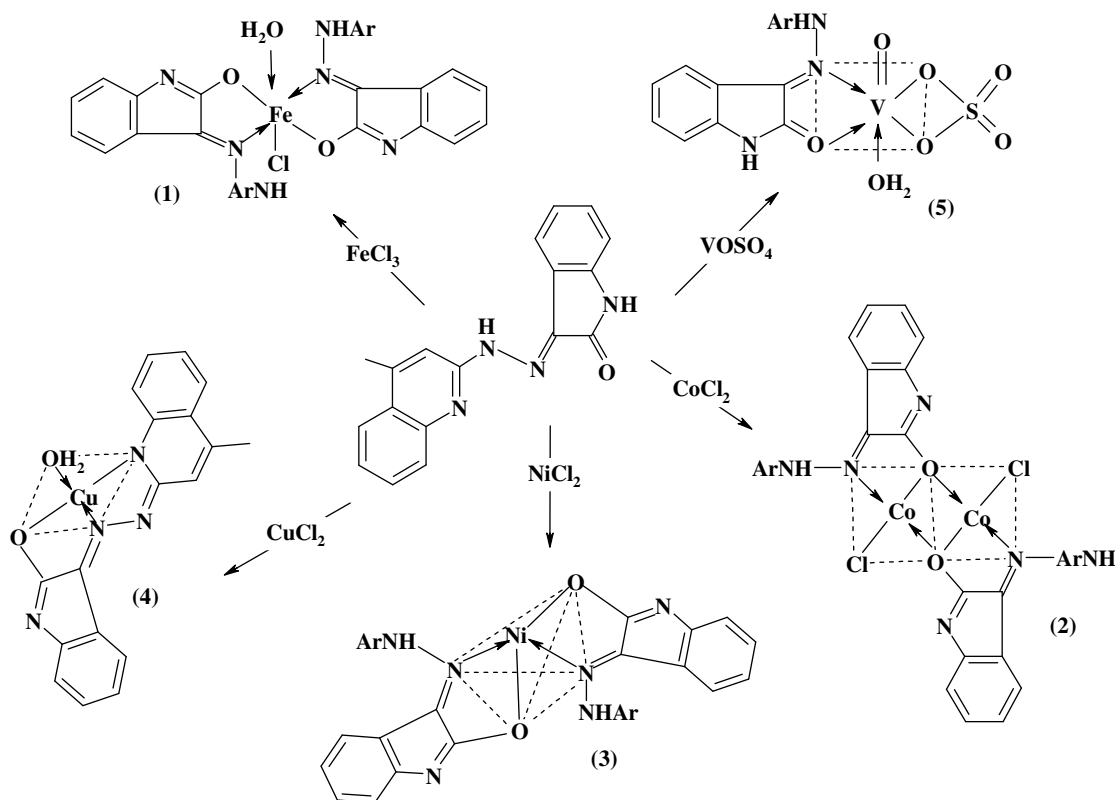
No.	Complex (F.W.)	Color	% Yield	$\mu_{\text{eff}}$ (B.M.)	$\lambda$ (nm)	Elemental Analysis; % Found/(Calcd.)			
						C	H	N	M
1	[Fe(HL) <sub>2</sub> (H <sub>2</sub> O)(OH)] (693.58)	Brownish orange	78	5.97	507	62.39 (62.34)	4.14 (4.22)	16.16 (16.16)	8.13 (8.00)
2	[Co(L)] <sub>2</sub> . $\frac{3}{4}$ H <sub>2</sub> O .MeOH (764.11)	Chocolate brown	62	1.66	504	58.23 (58.16)	3.56 (3.50)	14.68 (14.67)	15.40 (15.22)
3	[Ni(HL)Cl] <sub>2</sub> . $\frac{1}{4}$ H <sub>2</sub> O . $\frac{3}{8}$ MeOH (857.60)	Brown	56	---	507	52.28 (52.34)	4.20 (4.00)	13.07 (13.07)	13.67 (13.59)
4	[Cu(HL)Cl] <sub>2</sub> . $\frac{1}{2}$ H <sub>2</sub> O (827.73)	Reddish brown	83	1.59	508	52.20 (52.23)	3.58 (3.54)	13.57 (13.54)	15.39 (15.36)
5	[VO(HL) <sub>2</sub> (H <sub>2</sub> O)] . $\frac{2}{3}$ H <sub>2</sub> O (725.95)	Bright deep green	72	1.86	508	59.62 (59.56)	4.45 (4.49)	15.42 (15.44)	---



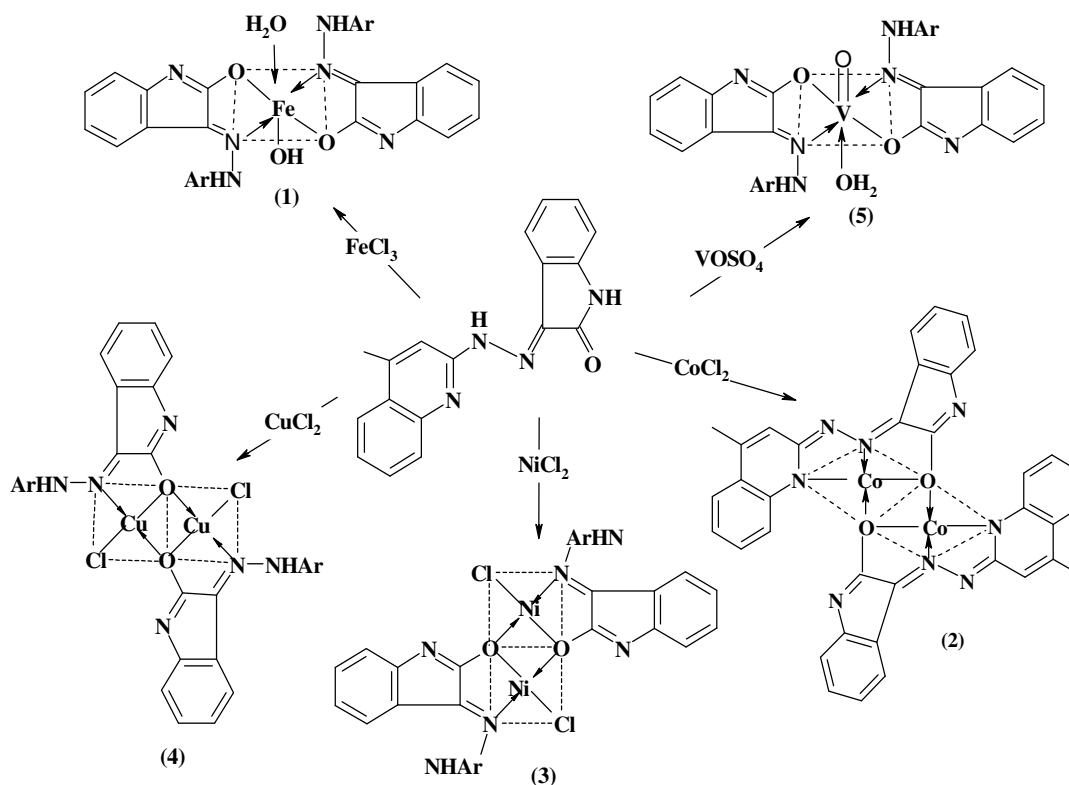
**Figure-1**  
**Electronic absorption spectra of the isatinic complexes in DMF**



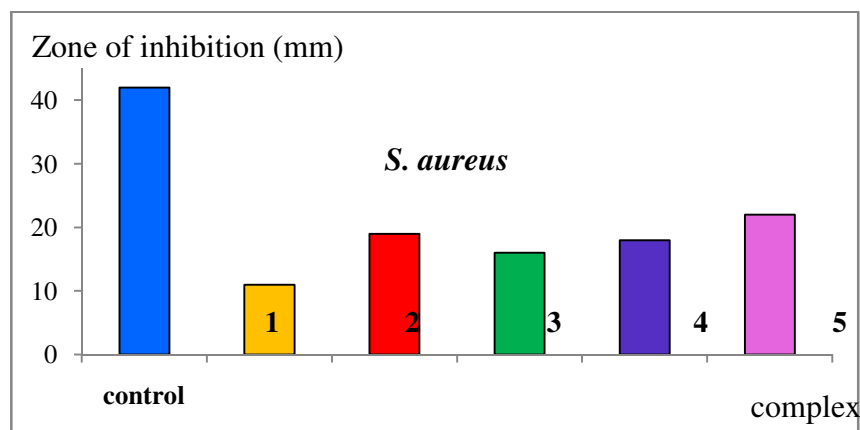
**Scheme-1**  
 Tautomeric forms of the isatinic hydrazone



**Scheme-2**  
 Reactions of  $H_2L$  with metal ions in absence of  $LiOH$  [Ref.7]



**Scheme-3**  
 Reactions of H<sub>2</sub>L with metal ions in presence of LiOH [current study]



**Figure-2**  
 Biological activity of the isatinic complexes

**ESR and Electronic Spectra:** The electronic spectra of the complexes as DMF solutions are nearly similar in terms of the position, intensity and shape of the bands (figure 1 and table 1). They showed new intense broad bands around 504-508 nm confirming their charge transfer (CT) nature. Therefore, the color of all complexes is dominated by a CT transition in the indole ring which obscured the weak d-d transitions occurring in the same region; a phenomenon encountered with isatinic complexes<sup>4-7</sup>. To our knowledge, the indole ring occurs in Orange blossoms and Jasmine flowers<sup>1</sup>. On the other side, the X-band ESR spectrum of a powdered sample of [VO(HL)<sub>2</sub>(H<sub>2</sub>O)] · 2½H<sub>2</sub>O; 5 gave a broad homogeneous signal centered on g = 2.19 without resolved hyperfine

structure; <sup>51</sup>V (I = 7/2, S = 1/2). The absence of vanadium's hyperfine coupling is common in the solid state and is attributed to the simultaneous flipping of neighboring electron spin or strong exchange interactions, which average out the interaction with the nuclei<sup>13</sup>. However the g- values show positive deviation from the g = 2.0023 (value of the free electron), indicating a covalent character in the M-L bonding<sup>12</sup>.

**Antimicrobial Activity:** The antimicrobial activity of the ligand and its metal complexes were summarized in table 2 and represented graphically in figure 2. Inspection of the data revealed that the ligand lacks the antimicrobial activity. Also, the antimicrobial activity is highly

influenced by the nature of the metal ion (figure 2) in consistency with our previous study<sup>7</sup>. The order for Gram-positive bacteria (*S. aureus*) is as follows: oxovanadium(IV) > Cobalt(II) > Copper(II) > Nickel(II) > Iron(III)

The investigated complexes exhibited low to moderate activities against *S. aureus* relative to the standard reference (control). In general, the antibacterial results (table 2), suggest low activity towards Gram-negative bacteria (*P. Phaseolicola*). In conclusion, the isatinic complexes gave a fair inhibitor effect on growth of the microorganisms and were more potent as bacteriostatic agents.

**Table-2**  
**Antimicrobial activity of the H<sub>2</sub>L and its complexes**

Complex	Zone of inhibition (mm)						Control #
	H <sub>2</sub> L	1	2	3	4	5	
<i>S. aureus</i>	---	11	19	16	18	22	42
<i>P. Phaseolicola</i>	---	--	3	--	4	6	36

## Conclusion

The ligational behavior of the isatinic hydrazone (H<sub>2</sub>L) is highly affected by the type of the metal ion as well as the pH of the reaction medium (scheme 3). The isolated copper(II)- and nickel(II)- complexes reflect the strong coordinating power of the Cl<sup>-</sup> anion in consistency with its donor number<sup>14</sup>. Due to the presence of LiOH in the reaction mixture, the isatinic hydrazone used its lactim form in all complexes. In case of cobalt (II)- and nickel(II)- complexes (2,3), the isatinic hydrazone produces ligand field strong enough to cause spin pairing. In summary, the base (LiOH) acts either as a deprotonating agent or as a coligand (complex 1) and enhances the dimerization (complexes 2-4).

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