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Synthesis, Spectroscopic and Antimicrobial Study of Transition Metal Complexes of 4-Hydroxy-3-Methoxybenzaldehyde and 2-Hydroxy-5-Nitrobenzaldehyde Semicarbazone

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ABSTRACT

Semicarbazones are compounds which are synthesized by condensation of semicarbazide hydrochloride and aldehydes or ketones. The literature survey revealed that semicarbazones had been emerged as a compound with broad range of activities including anticonvulsant, antitubercular, anticancer and antimicrobial activity. The aim of this study is to synthesis and characterization of 4-Hydroxy-3-methoxybenzaldehyde seimcarbazone Schiff base and its Nickel (II), Cobalt (II) complexes and 2-Hydroxy-5-nitrobenzaldehyde seimcarbazone Schiff base and its Nickel (II) complex. The results of FT-IR and UV-Vis spectra of the Schiff bases and metal complexes confirm the formation of azomethine group (C=N) accompanied with the absence of carbonyl group and the formation of new (M-N) and (M-O) bonds with all metal ions. The results assign that 4-Hydroxy-3-methoxybenzaldehyde seimcarbazone is neutral and bidentate species witch coordinated via azomethine N and O with both metal ions and 2-Hydroxy-3-methoxybenzaldehyde seimcarbazone is neutral tridentate species witch coordinated via azomethine N, O and OH group. The antimicrobial activity of Schiff bases and their metal complexes was carried out against four types of bacteria (Bacillus subtilis, Pseudomonas aeruginosa, Staphylococcus aureus and Escherichia coli) and one fungus (Candida ablicans) by using disc diffusion method. The results showed that the two Schiff bases were active against four tested organisms. The Nickel (II) complex of 4-Hydroxy-3-methoxybenzaldehyde seimcarbazone was active against one type of bacteria (Pseudomonas aeruginosa) and partially active against three type of bacteria (Escherichia coli, Staphylococcus aureus and Bacillus subtilis) and one fungus (Candida albicans) and Cobalt (II) complex of 4-Hydroxy-3-methoxybenzaldehyde seimcarbazone was partially active against one type of bacteria (Staphylococcus aureus) and one fungus (Candida albicans) and inactive against three type of bacteria (Escherichia coli, Pseudomonas aeruginos and Bacillus subtilis). And Nickel (II) complex of 2-Hydroxy-5-nitrobenzaldehyde seimcarbazone was partially active against two type of bacteria (Escherichia coli, Pseudomonas aeruginos) and one fungus (Candida albicans) and inactive against two types of bacteria (Pseudomonas aeruginosa and Bacillus subtilis).

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Introduction

Schiff bases were discovered in 1864 by German chemist and Nobel Prize winner Hugo Schiff. They are condensation products of primary amines and carbonyl compounds. Schiff bases are crucial in the field of coordination chemistry, given their remarkable ability to interact with and form stable complexes with nearly all metal ions. This versatility positions them as a primary organic ligand in this field. Schiff bases find extensive applications across various disciplines, including analytical and inorganic chemistry, as well as biological, medicinal and pharmacological areas. Additionally, Schiff bases are not only significant in biological systems but also used in the manufacturing of as catalysts, pigments and dyes, intermediates, and polymer stabilizers, corrosion inhibitors. Furthermore, they are employed in ion-selective electrodes for ion sensing [1].

Presently, bio-ligand synthesis is a growing interest of chemists in the field of coordination chemistry and their metal complexes with potential biological activity are the focus of extensive investigations. Schiff bases have been often used as chelating ligands in coordination chemistry, in catalysis, anti-oxidative activity, medicine as antibiotics, anti-inflammatory agents and in industry for anti-corrosion properties [2,3]. They are useful for preparation of pigments, dyes, catalysts, organic and inorganic synthesis, polymer stabilizers, and optical sensors [4,5]. Recently, the design and synthesis of metal complexes with Schiff base ligands have been attracted considerable attentions due to their ubiquitous applications in medicine, biological systems, and industries [6,7]. They are used as oxidation inhibitors for lubricating oils, and in the preparation of fluorescent brightener and liquid crystal compositions in optical sensors [8]. Furthermore, Schiff base complexes are used as the highly efficient catalyst for many organic transformations such as carbonylation, hydroformylation, reduction, oxidation, epoxidation, and hydrolysis. The mechanism of these transformations may proceed via cooperative binuclear complexes [9,10]. So, the transition metal Schiff base complexes containing two or more metal centers are suitable candidates for preparation of the highly efficient catalysts. It is also well known that coordination of a ligand to metal ion acts synergistically to increase the biological activity of the ligand and decreases the cytotoxic effects of metal ion and ligand [11].

In this study, we have synthesized and characterized 4-Hydroxy-3-methoxybenzaldehyde semicarbazone Schiff base and its complexes with Ni(II), Co(II) and 2-Hydroxy-5-nitrobenzaldehyde seimcarbazone Schiff base its complex with Ni(II). The prepared ligands and their complexes were screened against bacterial and fungal strains.

Materials and Methods

Chemical and Solvents

Semicarbazide hydrochloride, Ethanol, 2-Hydroxy-5-nitrobenzaldehyde, Vanillin (4-Hydroxy-3-methoxybenzaldehyde), Nickel (II) Chloride Hydrate and Cobalt (II) Chloride Hydrate.

Tools and Equipment's

Magnetic Stirrer, Reflux condenser, Sensitive balance, Petri dishes, Filter paper, Beakers, Funnel, Incubator, Micropipette, Test tube, FT-IR Spectrophotometer 8400 Japan (Shimadzu) and UV-Vis Spectrophotometer 1800 Japan.

Synthesis of 4-Hydroxy-3-Methoxybenzaldehyde Semicarbazone

Vanillin (4-Hydroxy-3-methoxybenzaldehyde) semicarbazone was prepared by refluxing semicarbazide hydrochloride with vanillin in (1:1 ratio) for 3 hrs. semicarbazide (0.557g, 0.005m) in hot ethanol (50ml) and vanillin (0.760g, 0.005m) in hot ethanol (20ml) were mixed the reaction mixture was refluxed for 3 hrs. The condensation product was filtered, recrystallized form ethanol and dried. The yield was 49.4%

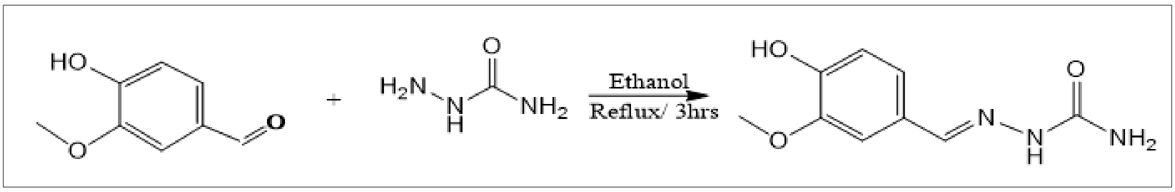
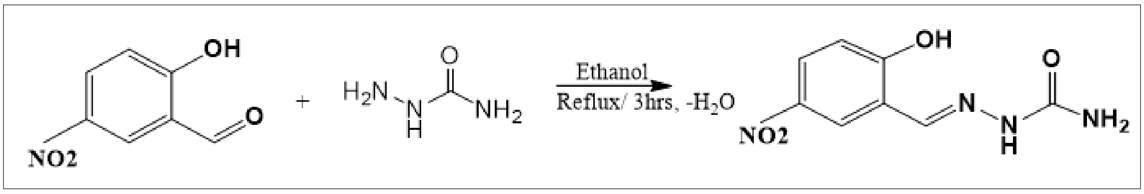


Figure 1: Synthesis of 4-Hydroxy-3-methoxybenzaldehyde semicarbazone.

Synthesis of 2-Hydroxy-5-Nitro Benzaldehyde Semicarbazone

2-Hydroxy-5-Nitro benzaldehyde semicarbazone was prepared by refluxing semicarbazide hydrochloride with 2-Hydroxy-5-Nitro benzaldehyde in (1:1 ratio) for 3 hrs. semicarbazide (0.557g , 0.005m) in hot ethanol (50ml) and vanillin (0.835g, 0.005m) in hot ethanol (20ml) were mixed the reaction mixture was refluxed for 3 hrs. The condensation product was filtered, recrystallized form ethanol and dried. The yield was 69.01%



Synthesis of 4-Hydroxy-3-Methoxybenzaldehyde Nickel (II) and Cobalt (II)Complexes

The Ni (II) and Co (II) complexes were prepared by addition of hot ethanolic solution of $NiCl_2.6H_2O$ (0.2377g, 0.001mmol) or $CoCl_2.6H_2O$ (0.2379g, 0.001mmol) drop wise separately to a refluxing ethanolic solution of the ligand (0.4183g, 0.002mmol,) until the metal:ligand ratio reached 1:2. The reaction mixture was maintained at the refluxing temperature for 3 hrs. The solid separated was filtered out, washed with ethanol and dried. The yield was 49.01% and 36.11% for Nickel and Cobalt complexes respectively.

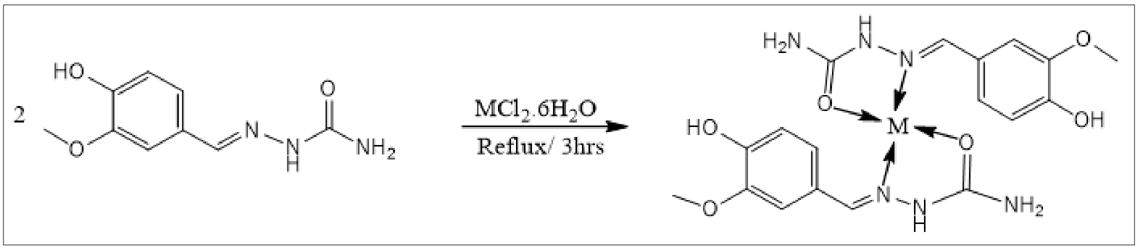


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Figure 3: Synthesis of 4-Hydroxy-3-methoxybenzaldehyde semicarbazone Nickel (II) and Cobalt (II) complexes:

Synthesis of 2-Hydroxy-5-Nitro Benzaldehyde Semicarbazone Nickel (II) and Cobalt (II) complexes

The Ni (II) complex was prepared by addition of hot ethanolic solution of the $NiCl_2.6H_2O$ (0.2377g, 0.001mmol) drop wise separately to a refluxing ethanolic solution of the ligand (0.4483g, 0.002mmol,) until the metal:ligand ratio reached 1:2. The reaction mixture was maintained at refluxing temperature for 3 hrs. The solid separated was filtered out, washed with ethanol and dried. The yield was 35.80%

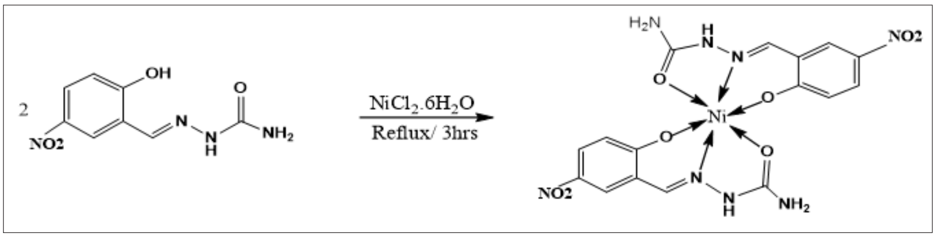

Figure 4: Synthesis of 2-Hydroxy-5-Nitrobenzaldehyde semicarbazone Nickel(II) complex

Chemical Analysis

FT-IR Analysis

The sample was mixed with potassium bromide and pressed under high pressure. The KBr melts and seals the sample into a matrix; the resulted KBr pellet that can be inserted into a holder in Perkin-Elmer FT-IR 8400 Japan (Shimadzu) spectrophotometer in wave number region 4000-200cm-1.

UV Analysis Assay

0.01g of sample dissolved in 5ml of ethanol, serial dilution many times was made then 1ml of solution placed into sample cell of UV spectrometer-1800-Shimadzu-Japan.

Testing of antibacterial susceptibility (Disc Diffusion Method)

Paper disc diffusion method was used to screen the antibacterial activity of the prepared compounds was performed by using Mueller Hinton agar (MHA). The experiment was carried out according to the National Committee for Clinical Laboratory Standards Guidelines (NCCLS, 1999). Bacterial suspension was diluted with sterile physiological solution to 108cfu/ ml (turbidity = McFarland standard 0.5). One hundred microliters of bacterial suspension were swabbed uniformly on surface of MHA and the inoculums were allowed to dry for 5 minutes. Sterilized filter paper discs (Whatman No.1, 6 mm in diameter) were placed on the surface of the MHA and soaked with 20 µl of a solution of each compound. The inoculated plates were incubated at 37°C for 24 hrs in the inverted position. The diameters (mm) of the inhibition zones were measured. The antibacterial activity results were expressed in term of the diameter of zone of inhibition and <9mm zone was considered as inactive; 9-12mm as partially active; while 13-18mm as active and >18mm as very active [12].

Results and Discussion

Some Physical Properties of the Ligands and their Metal Complexes

The UV-Vis spectra of Schiff bases under study was shown in Table 1: The band at 285 (λmax) due to the (π-π*) transition and band at 309 to 677(λmax) due to the (n-π*) transition for L1 and L2 respectively. The Ni(II) L1 complex showed band at 285 (λmax) due to the (π-π*) transition and band at 311(λmax) due to the (n-π*) transition. The Co(II) L1 complex showed band at 285(λmax) due to (π-π*) transition and band at 309(λmax) due to the (n-π*) transition. And for Ni (II) L2 complex showed band at 248(λmax) due to the (π-π*) transition and band at 317(λmax) due to the (n-π*) transition.

Table 1: Some Properties and UV-Vis Spectrum of the Schiff Bases and Their Complexes:

No	Compounds	Ratio	Yield	Color	n-π* (nm)	π-π* (nm)
1	L1	1:1	49.4%	Yellow	338	285
2	L2	1:1	69.01%	Yellow	677	285
3	Ni(II) complex	1:2	49.01%	White	311	285
4	Co(II) complex	1:2	36.11%	White	309	285
5	Ni(II) complex	1:2	35.80%	Yellow	317	248

IR Spectra of the Ligand and their Metal Complexes

The IR spectra of the ligand L1 and its Nickel (II) and Cobalt (II) complexes are shown in table 2. The IR spectra of the ligand showed bands at 3295 and 3294 cm^{-1} which are assigned to $\nu(NH_2)$ and ν(NH) respectively [13]. these data suggested that the ligand is coordinating to the metal center in the neutral form [14]. The azomethine ν(C=N)) is shifted to lower frequency from 1612 to 1602 cm^{-1}, in both complexes indicating the coordination of the azomethine nitrogen [15]. And the bands from 3442-3481 are due to ν(OH) in the ligand and it is metal complexes. New bands appeared at 505 and 559 are due to ν((M-N) and bands at 619 and 615 are due to ν((M-O) in Nickel(II) and Cobalt(II) complexes respectively.

The IR spectra of the ligand L_2 and its Nickel(II) complex are shown in table 2. The IR spectra of the ligand showed bands at 3149 and 3089 cm^{-1} which are assigned to ν(NH_2) and ν(NH) respectively [13]. these data suggested that the ligand is coordinating to the metal center in the neutral form [14]. The azomethine ν(C=N)) is shifted to lower frequency from 1602 to 1600 cm^{-1}, indicating the coordination of the azomethine nitrogen. And the band at 3479 is due to ν(OH) in the ligand. New bands appeared at 570 is due to ν((M-N) and band at 536 is due to ν((M-O) in Nickel (II) complex [15].

Table 2: IR Bands (cm-1) of Semcarbazone Ligands and their Metal Complexes:

No	Compounds	Wave number (cm^{-1})						
		ν(C=N)	ν(C=O)	ν(NH2)	ν(NH)	ν(OH)	ν((M-N)	ν(M-O)
1	L1	612	1687	3294	3295	3463	-	-
2	L2	602	1701	3149	3089	3481	-	-
3	Ni(II) complex	1602	-	3296	3072	3442	505	619
4	Co(II) complex	1602	-	3296	3070	3456	559	615
5	Ni(II) complex	1600	-	3149	3091	-	570	636

Antimicrobial activity of Ligand and its Metal Complexes
The two ligands were active against four tested bacteria (Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis and Staphylococcus aureus) and one fungus (Candida albicans). The Nickel (II) complex of L_1 was active against one type of bacteria (Pseudomonas aeruginosa) and partially active against three type of bacteria (Escherichia coli, Staphylococcus aureus, Bacillus subtilis) and one fungus (Candida albicans) and Cobalt (II) complex of L_1 was partially active against one type of bacteria (Staphylococcus aureus) and one fungus (Candida albicans) and inactive against three type of bacteria (Escherichia coli, Pseudomonas aeruginos and Bacillus subtilis) and the Nickel (II) complex of L_2 was partially active against two type of bacteria (Escherichia coli, Pseudomonas aeruginos) and one fungi (Candida albicans) and inactive against two type of bacteria (Pseudomonas aeruginosa and Bacillus subtilis) and As shown in Table 3

Table 3: Antimicrobial Activity of Semcarbazone Ligands and their Metal Complexes

No	Compounds	Gram-ve Bacteria		Gram+ve Bacteria		v
		E. coli	Ps.a	S.a	B.s	Ca
1	L_1	15	16	14	13	18
2	L_2	14	16	16	18	20
3	Ni (II) complex	12	14	10	11	10
4	Co (II) complex	09	09	10	-	11
5	Ni (II) complex	10	-	12	-	10

Key: <9mm zone was considered as inactive; 9-12mm as partially active; while 13-18mm as active and >18mm as very active.

Conclusion
Semicarbazones are important compounds obtained by condensation of semicarbazides with suitable aldehyde or ketones, semicarbazone ligands coordinate to transition metals through oxygen and nitrogen donor atoms in their (N,O) bidentate or (N,O,O) tridentate forms, to from naturals complexes. The reaction of Schiff bases ligands with the metal ions at a 1:1 ligand to metal ratio yielded monomeric complexes, which are structurally characterized using several physicochemical techniques. The analysis suggested coordination environments of four and six-coordinate geometries for the metal complexes. Finally, antibacterial and antifungal of Schiff bases ligands and their complexes were evaluated.

Conflict of Interest
The authors declare that they have no conflict of interest.

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