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SYNTHESIS, SPECTROSCOPIC INVESTIGATION AND BIOEFFICACY OF SOME NOVEL SCHIFF BASE METAL (II) COMPLEXES

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Keywords:

Schiff base metal complexes, XRD study, Antibacterial, DNA cleavage and antioxidant activity

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ABSTRACT: Two monobasic bidentate ligands L^1H [2-(5-Bromo-2-dihydro-2-oxo-1*H*-indol-3-ylidene)hydrazine-carboxamide] and L^2H [2-(5-Bromo-2-dihydro-2-oxo-1*H*-indol-3-ylidene)hydrazinecarbothioamide] were synthesized by the condensation of [2-(5-Bromo-2-dihydro-2-oxo-1*H*-indol-3-ylidene) with semicarbazide and thiosemcarbazide, which formed a series of complexes with cobalt(II) and nickel(II). The ligands and the metal complexes were characterized based on elemental analysis, IR, UV–Visible, ^{1}HNMR, Mass spectroscopy. Spectral studies revealed that the ligands acted as monobasic bidentate, coordinating to the metal ion through the azomethine nitrogen *i.e.* >C=N and carbonyl oxygen atom of the isatin moiety. All the Schiff base metal complexes have a mononuclear structure, and the octahedral geometry has been proposed on the basis of spectral studies. The nickel (II) complex Ni (L^2) (OAc).$3H_2O$ was subjected to XRD studies which revealed a monoclinic crystal system. *In vitro*, biological screening effects of the compounds were tested against two bacterial species *Staphylococcus aureus* and *Escherichia coli*. DNA cleavage and antioxidant activity of the ligands and their respective complexes were also examined.

INTRODUCTION: In coordination chemistry, Schiff bases have an important role as ligands. Schiff bases form an important class of the most widely used organic ligands and have a variety of applications in many fields, including inorganic, biological and analytical chemistry. Isatin (2, 3-dioxoindole or indole- 2, 3-dione) based Schiff base ligands and their derivatives are a unique compound identified in humans, and its effect has been studied in a variety of systems. The biological properties of isatin include a range of actions in the brain and offer protection against certain types of infections. Isatin-based Co (II) and Ni (II) compounds have a range of actions, such as CNS-MAO inhibition [1], anticonvulsant [2].

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Many isatin derived compounds possess a wide spectrum of medicinal properties and thus have been studied for activity against the tumor, tuberculosis, antioxidant, leprosy, fungal, viral and bacterial infections, *etc*. [3-13] Apart from biological activities, they are also used in organic synthesis, dyes, pigments, polymer stabilizers, corrosion inhibitors, fungicidal, agrochemical ion exchange, nonlinear optics and industrial catalysis [14-16].

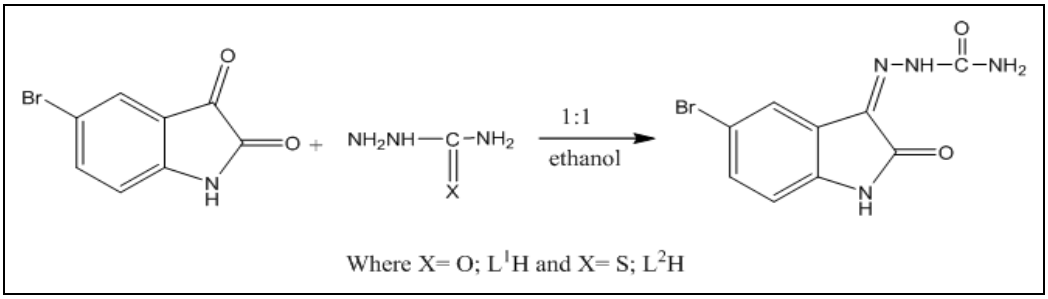
As a part of our work on isatin derivatives, herein we report the synthesis of transition metal complexes derived from L^1H [2-(5-Bromo-2-oxo-1H-indole-3-ylidene) hydrazinecarboxamide] and L^2H [2-(5-Bromo-2-dihydro-2-oxo-1H-indole-3-ylidene) hydrazincarbothioamide]. These compounds were characterized by elemental analysis, spectroscopic techniques (IR, UV-VIS and ^{1}HNMR), and XRD studies. They have been evaluated for antibacterial, DNA cleavage, and antioxidant activity and the results are indeed positive.

EXPERIMENTAL SECTION:

Materials: All the chemicals (reagent grade) and solvents (analytical grade) were distilled over appropriate drying agents immediately before use. 5-Bromo-indole-2, 3-dione, cobalt, and nickel acetate salts were purchased from Sigma-Aldrich and used as purchased without further purification.

Physical Measurements: The molecular weights were determined by the Rast's camphor method [17]. Sulfur and nitrogen were estimated by Messenger's [18] and Kjeldahl's [19] methods, respectively. The melting points were determined on an electrical melting point apparatus. IR spectra of the Schiff base ligands and their metal complexes were recorded using the Shimadzu FTIR-8400s instrument (KBr pellet technique). The ^{1}H NMR spectra of the ligands are obtained on a JEOL ECS 400 MHz NMR spectrometer, MNIT (Jaipur). Dimethylsulfoxide, (DMSO–d6) was used as a solvent and tetramethylsilane (TMS) as an internal reference. The powder X-ray diffraction measurements were performed at the MNIT (Jaipur) on a Panalytical Xpert Pro 3040 instrument (wavelength = 1.54 Å). Mass spectra were obtained on Xevo G2-S Q Tof (Waters, USA), MNIT, Jaipur.

Preparation of Ligands: To prepare ligand (L^1H), 3.0 g (1.32mmol) of [2-(5-Bromo-2-dihydro-2-oxo-1*H*-indol-3-ylidene) and 1.48 g (2.6 mmol) of semicarbazide hydrochloride was dissolved in ethanol (100 mL) in the presence of sodium acetate (1.10 g, 1.32mm) and to prepare ligand (L^2H) 3.0 g (1.32mmol) of [2-(5-Bromo-2-dihydro-2-oxo-1*H*-indol-3-ylidene) and 1.20g (1.31 mmol) of thiosemicarbazide was dissolved in ethanol at the molar ratio 1:1 (**Scheme 1**). The mixtures were refluxed for 5-6 h. After that, the solid product was filtered off, washed several time with ethanol, recrystallized from ethanol, and finally dried under vacuum over fused calcium chloride.

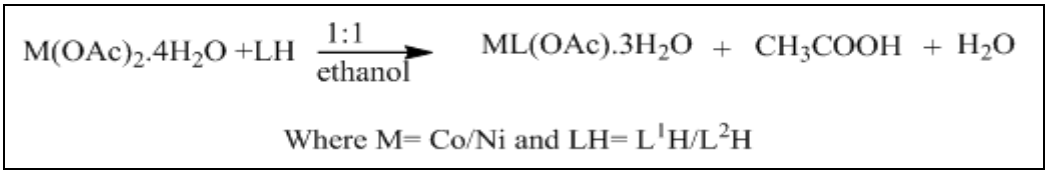


Where X= O; L^1H and X= S; L^2H

SCHEME 1

Synthesis of Metal Complexes:

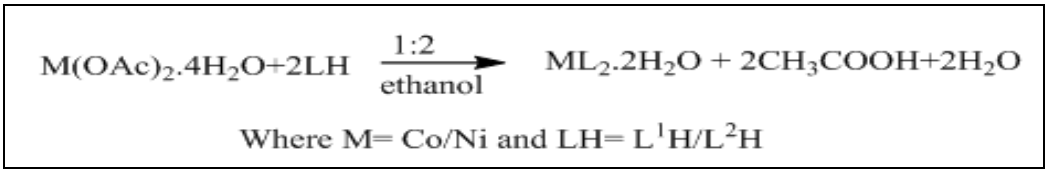
Synthesis of Metal Complexes of L^1H and L^2H (1:1): An aqueous ethanolic solution (25cm^3) of Co(II) acetate (0.94 g, 3.70 mmol) and Ni(II) acetate (0.94 g, 3.70 mmol) was added to a boiling ethanolic solution of the ligand L^1H and L^2H (1.76 g, 3.76 mmol) to cause precipitation (**Scheme 2**).



Where M= Co/Ni and LH= L^1H/L^2H

SCHEME 2

Synthesis of Metal Complexes of L^1H and L^2H (1:2): An aqueous ethanolic solution of Co(II) (0.47 g, 1.85 mmol) and Ni(II) (0.47 g, 1.85 mmol) acetates was added to a boiling ethanolic solution of the ligands L^1H and L^2H (1.76 g, 3.76 mmol) to cause immediate precipitation (**Scheme 3**).



Where M= Co/Ni and LH= L^1H/L^2H

SCHEME 3

The resulting mixture was heated under reflux for 7–8 h on glass apparatus fitted with quick fit interchangeable standard ground joints. After the reaction was complete, the solvent was removed under reduced pressure, and the solid product was washed with warm water & aqueous ethanol to remove unreacted metal acetate or ligands and recrystallized from ethanol. The purity was checked by thin-layer chromatography using silica gel-G as the stationary phase. $_{i}Co(L^{1})(OAc)\cdot 3H_2O$,$_{i}Co(L^{1})_2\cdot 2H_2O$, $iNi(L^{1})(OAc)\cdot 3H_2O$,$_{i}Ni(L^{1})_2\cdot 2H_2O$,$_{i}Co(L^{2})(OAc)\cdot 3H_2O$,$_{i}Co(L^{2})_2\cdot 2H_2O$,$_{i}Ni(L^{2})(OAc)\cdot 3H_2O$,$_{i}andiNi(L^{2})_2\cdot 2H_2O$ complexes were synthesized.

Biological Activity Testing:

Antibacterial Activity: The antibacterial activity testing of ligands $L^{1}H$, $L^{2}H$, and their Schiff base metal complexes against *Staphylococcus aureus* (ATCC 29213) and multidrug-resistant strain of *Escherichia coli* (ESBL) (ATCC 35218) was performed by disk diffusion method [20-21].

Different concentrations of the test compounds under study were prepared from the stock solution and then the dilution series was prepared for the compound, out of which 50 µL was used in each well. Streptomycin was used as a positive control (5 mg/mL concentration) for antibacterial activity. Mueller-Hinton agar medium is the only susceptibility test medium that has been validated by CLSI for screening the antibacterial activity by disk diffusion susceptibility testing. Cultures of *Staphylococcus aureus* (ATCC 29213) and multidrug-resistant strain of *Escherichia coli* (ATCC 35218) were inoculated in peptone water and were kept for incubation for 30 min at 37°C. The bacterial suspensions were compared to 0.5 McFarland turbidity standard [22]. Bacterial cultures were swabbed onto the Mueller Hinton Agar surface onto the Saboraud Dextrose Agar surface. 50 µL from different dilutions prepared from stock (100mg/mL and 50mg/mL of the compound) was loaded into the respective wells. The antibacterial plates were kept for incubation at 37°C for 24 h.

The % activity indices for the test compounds were calculated by the formula:

$$\% \text{ Activity Index} = Z_{test} \times 100\% / Z_{standard}$$

Here Z_{test} is the zone of inhibition of test compounds (diameter in mm) and $Z_{standard}$ is a zone of inhibition of standard compounds (diameter in mm).

DNA Cleavage Activity Testing: DNA cleavage [23] study was conducted in three main steps:

I. Treatment of *Pseudomonas Aeruginosa* with Compounds: *Pseudomonas Aeruginosa* (ATCC – 27853) strain was used for this work. The stock solution of the compounds were prepared by mixing 590 mg of each compound in 3.5 mL of ethanol. Two concentrations, 1 mg/mL and 10 mg/mL were used in this experiment. For 10 mg/mL, 180 µL of stock solution of compounds mixed with 3 mL of autoclaved LB broth test tube. For 1 mg/mL 18 µL was added into 3 mL LB broth. After mixing of compounds in LB broth, 1% of *Pseudomonas Aeruginosa* was inoculated in LB broth and incubated for 24 hrs mixed in both the 10 mg and 1 mg concentration test tubes. Test tubes were kept in the incubator for 48 h in 37°C.

II. Isolation of Genomic DNA of *Pseudomonas Aeruginosa* Treated with Compounds: After 48 h of incubation 1.5 mL of broth centrifuged at 10000 rpm for 10 minutes to settle down the cells. 600 µL of TNES buffer and 15 µL of proteinase-K (20 mg/mL) were added into the pellet. Resuspended the pellet by inverting the tube several times. The sample was placed on a water bath. The samples were incubated overnight at 50^{O}C. Occasionally we mixed the samples by inverting the tubes and making sure the lids are snapped shut as they can sometimes pop loose when warm. After overnight incubation 500µL of phenol: chloroform (1:1) were added and mixed properly by inverting the tube several times. The tubes were centrifuged at 10000 rpm for 10 minutes at 4°C. After centrifugation, the aqueous layer was transferred into a fresh tube. 166.7 µL of 6M NaCl was added. The samples were shaken vigorously for 20 seconds. The samples were centrifuged at 12-14,000 rpm for 5-10 minutes at room temperature. The supernatant was removed to a new, labelled tube. An equal volume (~ 800 µL) of cold 100 % ethanol was added and gently mixed by inverting the tube a couple of times; at this step, white DNA precipitate was seen out of the solution. The samples were centrifuged at 12-14,000 rpm for 10-20 min at 4°C. [Room temperature will suffice if there is plenty of DNA]. The supernatant was poured off, taking care

not to dislodge the pellet of DNA. DNA pellet was washed with 70% ethanol. After removing the 70% ethanol, the samples were briefly centrifuged to get the last traces of the ethanol at the bottom of the tube; the remaining ethanol was pipetted off. The sample left to air dry, it usually takes 10-30 min depending upon the temperature. As soon as the sample was just dry, The DNA in 50 µL of Tris-EDTA was re-suspended.

III. Qualitative Analysis of DNA by Agarose Gel Electrophoresis:

Preparation of Stock Solution of TAE Buffer: EDTA solution (pH 8.0, 0.5M) was prepared by weighing 9.31g of EDTA and it was dissolved in 40mL distilled water. EDTA is insoluble and it can be made soluble by adding sodium hydroxide pellets. The pH was checked using a pH meter. The solution was made to 100mL by adding distilled water.

DNA Cleavage Analysis: After the cleavage of the DNA with the chemical treatment at 5 mg/mL concentration the banding pattern was analyzed by Agarose gel electrophoresis using 1.2% Agarose gel. The cleavage pattern was detected after 48 h and 96 h of incubation; the bands were visualized on a UV-trans illuminator. DNA ladder was used 100-1000bp (100 bp step up the ladder, Merck).

Antioxidant Activity: Antioxidant activity was done by DPPH scavenging [24] methods. For this standards were prepared by DPPH antioxidant. L^1H & L^2H ligands and Schiff base metal compounds *i.e.* Co $(L^1)_2.2H_2O$, Ni $(L^1)_2.2H_2O$, Co $(L^2)_2.2H_2O$, Ni $(L^2)_2.2H_2O$ were analyzed for antioxidant activity by DPPH (Standards = Ascorbic Acid). The stock solution of extracts was prepared and 1 mL stock solution of the extract with different concentrations was taken in a test tube. Then 1mL DPPH was added to the extract and the tubes were incubated for 10min in dark at room temperature. After 10 min. of incubation, O.D. at 517nm was recorded.

(% Inhibition) was calculated with the help of the following formula;

DPPH Scavenging Activity (% Inhibition) = (OD of Control – OD of Sample) × 100 / OD of Control
(*Control = DPPH)

RESULTS AND DISCUSSION: Schiff base ligands L^1H [2-(5-bromo-2-dihydro-2-oxo-1H-indole-3-ylidene) hydrazinecarboxamide] and L^2H [2-(5-Bromo-2-dihydro-2-oxo-1H-indole-3-ylidene) hydrazinecarbothiamide] were synthesized by the reaction of [2-(5-Bromo-2-dihydro-2-oxo-1H-indol-3-ylidene) with hydrazinecarboxamide (in the presence of the reaction of sodium acetate) and hydrazinecarbothioamide in a 1:1 molar ratio in absolute ethanol, respectively **Fig. 1**. The synthesized Co(II) and Ni(II) Schiff base complexes are solids soluble in ethanol, DMSO and benzene. In **Table 1** the analytical data for Schiff base ligands and their metal complexes *i.e.* $_i Co(L^1)(OAc)\cdot 3H_2O$, $_i Co(L^1)_2\cdot 2H_2O$, $_i Ni(L^1)(OAc)\cdot 3H_2O$, $_i Ni(L^1)_2\cdot 2H_2O$, $_i Co(L^2)(OAc)\cdot 3H_2O$, $_i Co(L^2)_2\cdot 2H_2O$, $_i Ni(L^2)(OAc)\cdot 3H_2O$, and $_i Ni(L^2)_2\cdot 2H_2O$ are summarized.

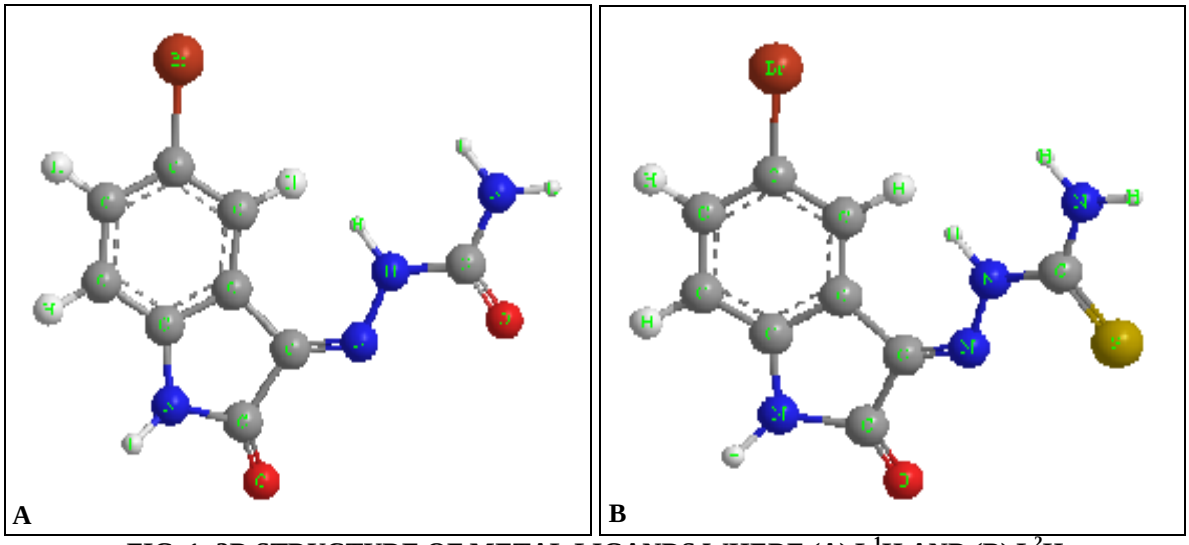


FIG. 1: 3D STRUCTURE OF METAL LIGANDS WHERE (A) L^1H AND (B) L^2H

TABLE 1: ANALYTICAL DATA AND PHYSICAL PROPERTIES OF THE LIGANDS AND THEIR COMPLEXES

Compound	Colour	MP (°C)	Elemental Analysis Data												Moler Mass; Found/ Calculated
			Found%						Calculated%						
			C	H	N	S	Ni	Co	C	H	N	S	Ni	Co	
L^1H	Pale yellow	279	37.98	2.09	19.54	-	-	-	38.19	2.49	19.79	-	-	-	281.79/283.31
L^2H	Reddish-brown	265	35.91	2.20	18.02	10.23	-	-	36.14	2.36	18.73	10.72	-	-	299.01/299.37
$Co(L^1)(OAc)\cdot 3H_2O$	yellow	292	28.72	3.01	12.08	-	-	12.13	29.10	3.33	12.34	-	-	12.98	454.06/454.099
$Co(L^1)_2\cdot 2H_2O$	Orangish brown	299	32.28	2.14	16.60	-	-	8.23	32.80	2.45	17.00	-	-	8.94	659.02/659.11
$Ni(L^1)(OAc)\cdot 3H_2O$	Dark yellow	265	28.81	3.11	11.98	-	12.76	-	29.11	3.33	12.34	-	12.93	-	453.62/453.85
$Ni(L^1)_2\cdot 2H_2O$	Marigold yellow	312	32.13	2.21	16.87	-	8.65	-	32.81	2.45	17.01	-	8.91	-	658.63/658.87
$Co(L^2)(OAc)\cdot 3H_2O$	Dark pink	297	27.91	3.10	11.67	6.16	-	6.34	28.10	3.22	11.92	6.82	-	6.82	468.71/468.92
$Co(L^2)_2\cdot 2H_2O$	Rust orange	301	31.79	2.05	16.31	4.30	-	8.21	32.03	2.39	16.60	4.75	-	8.70	674.73/674.93
$Ni(L^2)(OAc)\cdot 3H_2O$	Dark Green	311	27.89	2.99	11.76	6.58	12.03	-	28.12	3.22	11.92	6.82	12.49	-	469.78/469.92
$Ni(L^2)_2\cdot 2H_2O$	Clay brown	303	31.89	2.10	16.21	4.39	8.24	-	32.02	2.39	16.60	4.74	8.73	-	659.78/659.89

The spectra of the ligands and their metal complexes helped to confirm the formation of complexes. For this, the IR spectra of Co(II) and Ni(II) complexes were compared with the ligands *i.e.* L^1H and L^2H are listed in **Table 2**. The bands at 1600-1615 cm^{-1} attributed to the =C=N group in the IR spectra of the free ligands shifted to lower wavenumbers in the spectra of the Co (II) and Ni (II) complexes, which suggests coordination of the azomethine nitrogen to the metal ion. The IR spectra of the free ligands display two sharp bands at 3440–3495 and 3320–3350 cm^{-1} due to the ν_{ass} and ν_s modes of the $-NH_2$ group, respectively.

These bands remain at almost the same positions in the spectra of the Schiff base metal complexes, suggesting that the $–NH_2$ group is not involved in complexation. The same relates to the isatin moiety *i.e.* the strong indole ν_{NH} band remains unaltered in the spectra of the ligands and complexes (3170–3180 cm^{-1}). Comparative analysis of the IR spectra of the metal complexes and ligands show the disappearance of the broadband at 3265–3286 cm^{-1} due to the ν_{NH} mode of semicarbazone and thio-semicarbazone ligands which shows deprotonation of this group on complexation. The $\nu_{(C=O)}$ or $\nu_{(C=S)}$ bands of semicarbazone or thiosemicarbazone moiety at, respectively, 1680–1695 and 1050–1075 cm^{-1} in the IR spectra of the ligands are shifted to lower wavenumbers in IR spectra of the complexes suggesting involvement of thiolic sulfur or carbonyl oxygen in coordination with the metal.

The band at 1720 cm^{-1} due to the isatin -C=O bond remains unaltered in the complexes, indicating non-involvement of carbonyl group in complexation. The bands at 540-585 and 410-465 cm^{-1} can be attributed to the $\nu_{(M–O)}$ and $\nu_{(M–N)}$ modes, respectively.

TABLE 2: IR VIBRATIONAL FREQUENCIES (cm^{-1}) FOR THE LIGANDS AND THEIR CORRESPONDING COMPLEXES

Compound	ν(NH)	ν(C=N)	ν(OCOCH3)	ν(M–N)	ν(M–O)	ν(H_2O/OH)
HL^1	3264	1611	-	-	-	-
HL^2	3269	1616	-	-	-	-
$Co(L^1)(OAc)\cdot 3H_2O$	-	1597	1725	452	510	3356
$Co(L^1)2\cdot 2H_2O$	-	1593	-	414	518	3352
$Ni(L^1)(Oac)\cdot 3H_2O$	-	1597	1724	412	527	3347
$Ni(L^1)2\cdot 2H_2O$	-	1595	-	418	532	3300
$Co(L^2)(Oac)\cdot 3H_2O$	-	1596	1727	462	-	3349
$Co(L^2)2\cdot 2H_2O$	-	1598	-	456	-	3359
$Ni(L^2)(Oac)\cdot 3H_2O$	-	1593	1726	420	-	3348
$Ni(L^2)2\cdot 2H_2O$	-	1598		422	-	3302

Mass Spectra: The EI mass spectrum of $[Ni(L^1)(Oac)3H_2O)]$ complex was studied as a typical case. The molecular ion peak of the $[Ni(L^1)(Oac)3H_2O)]$ complex was observed at m/z 452.95 and this is in good agreement with its molecular weight, which proposes the monomeric nature of the Ni (II) complex and confirms the proposed formula (see **Fig. 2**).

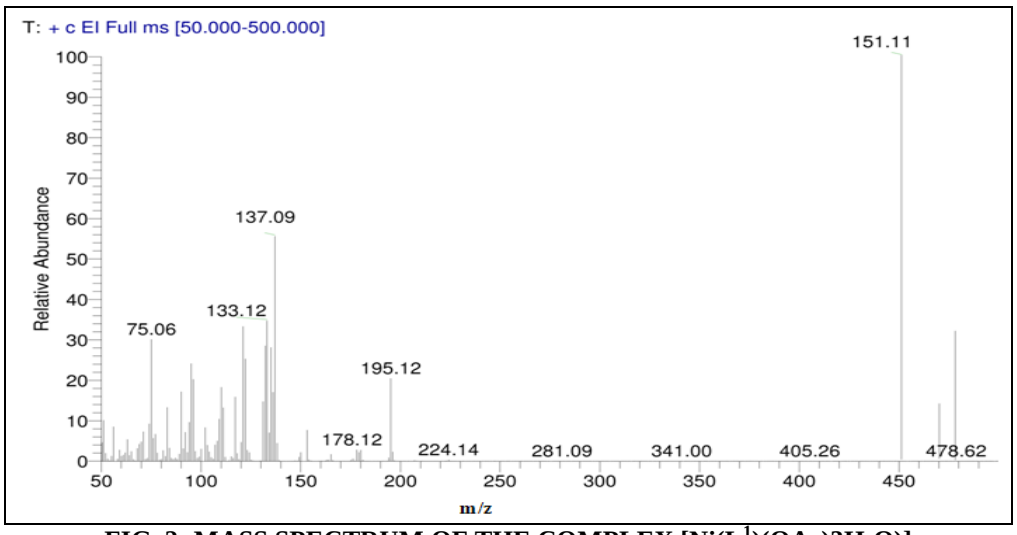


FIG. 2: MASS SPECTRUM OF THE COMPLEX [Ni(L^1)(OAc)3H_2O)]

NMR Spectra: ^{1}H NMR spectra of the ligands were recorded in DMSO-d_6 solution using TMS as the internal standard (see **Table 3**). The ligands L^1Hand L^2H exhibit –NH proton resonance signals at δ 10.47 and 11.27 ppm, respectively. A singlet at δ 11.01 and 12.35 ppm in free ligands is due to the -NH group of the indole ring. The signals observed at 3.12 and 3.72 ppm is due to the -NH_2 group in the spectra of HL^1 and HL^2, respectively. The spectrum of the ligand exhibited multiplet at 6.18-8.46 ppm due to aromatic protons.

TABLE 3: CHEMICAL SHIFT (δ, ppm) IN ^{1}H NMR SPECTRA OF THE LIGANDS

Compounds	-NH	-NH_2	-CH=N	Aromatic
HL^1	10.47 s	3.12	8.31	6.18-8.28
HL^2	11.27 s	3.75	8.35	6.87-8.46

Electronic Absorption Spectra: The electronic absorption spectra of Schiff base metal complexes were recorded in ethanol, which suggests an octahedral geometry for metal complexes. Three spin allowed transitions are possible for cobalt (II) and nickel (II) in an octahedral environment. The electronic spectra of cobalt (II) complexes characterized by three transitions;

$$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P) \quad 9260–9490\ cm^{-1}\ (\nu_1)$$
$$^4T_{1g}(F) \rightarrow {}^4A_{2g}(F) \quad 9425\text{-}20420\ cm^{-1}\ (\nu_2)$$
$$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P) \quad 21490\text{-}22001\ cm^{-1}\ (\nu_3)$$

Which indicate the octahedral stereochemistry of the complexes. The ligand field parameters (*Dq, B*, β, and β%) have been calculated for the Co (II) complexes by using the following equations-

$$\nu_2 = \nu_{1+}\ 10Dq$$
$$B = \nu_2 + \nu_3 - 3\ \nu_1 / 15\ ^{(25)}$$

The Racah parameter (*B*) is also calculated *i.e.* 870–935 cm^{-1} (< 971 cm^{-1}) suggesting an orbital overlap and delocalization of the electron on the metal ion. The six coordinated nickel (II) belongs to the electronic spectrum of an octahedral nickel (II) $3d^8$ system. The complex is expected to show three spin allowed transitions which are assigned as shown below-

$$^3A_{2g}(F) \rightarrow {}^3T_{2g}(F) \quad 9800–9950\ cm^{-1}(\nu_1)$$
$$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F) \quad 16200–16600\ cm^{-1}\ (\nu_2)$$
$$^3A_{2g}(F) \rightarrow {}^3T_{1g}(P) \quad 24800–25000\ cm^{-1}(\nu_3)$$

These transitions indicate octahedral geometry for the Ni (II) ion. By using the Band-fitting equation ligand field parameters have been calculated for Ni (II) complexes.

$$Dq = \nu_1/10$$
$$B = \nu_2 + \nu_3 - 3\ \nu_1 / 15$$

The Rachah parameter B for Co(II) and Ni(II) metal will be always less for the complexed ion than that for free ion *i.e.* 1041 cm^{-1}. The reduction of the value of this parameter in the Schiff base metal complex shows covalency in the metal-ligand bond. The value of β, nephelauxetic ratio, is a measurement of covalency. The nephelauxetic ratio (β) for the 1: 1 and 1: 2 cobalt and nickel complexes is less than one, which shows a partial covalent character. The values for Dq, B, β%, ν_2/ν_1 are listed in **Table 4**.

TABLE 4: ELECTRON TRANSITION FREQUENCIES AND LIGAND FIELD PARAMETERS OF THE METAL COMPLEXES

Compound	Frequency, cm^{-1}			Dq, cm^{-1}	B, cm^{-1}	ν_2/ν_1	β	β%
	ν_1	ν_2	ν_3					
$Co(L^1)(OAc)\cdot 3H_2O$	9267	19412	21471	1014.5	872.1	2.09	0.898	10.2
$Co(L^1)_2\cdot 2H_2O$	9321	19612	21510	1029.1	877.2	2.10	0.903	9.70
$Ni(L^1)(OAc)\cdot 3H_2O$	9911	15361	22750	991.1	558.5	1.54	0.536	46.4
$Ni(L^1)_2\cdot 2H_2O$	9991	15473	22839	999.1	555.9	1.54	0.534	46.6
$Co(L^2)(OAc)\cdot 3H_2O$	9468	19913	21810	1044.5	887.9	2.10	0.914	8.60
$Co(L^2)_2\cdot 2H_2O$	9459	20400	21900	1094.1	928.2	2.15	0.955	4.50
$Ni(L^2)(OAc)\cdot 3H_2O$	9921	15090	24849	992.1	678.4	1.52	0.651	34.9
$Ni(L^2)_2\cdot 2H_2O$	9947	15310	24855	994.7	688.2	1.53	0.661	33.9

X-Ray Powder Diffraction: The XRD of the Ni (II) complexes was scanned in the range 5–100° at a wavelength of 1.543 Å. The diffractograms and associated data represent the relative intensity, 2θ value for each peak and inter-planar spacing (d-values). The Ni (II) complex *i.e.* Ni (L^2) (OAc). $3H_2O$ was subjected for X-ray powder diffraction [26-27] studies (see **Fig. 4**) to find out the lattice dynamics of the metal complex. The structural studies reported that the crystal has a monoclinic system. The crystal data obtained was a=7.680Å b=4.320Å c=16.6256Å. **Tables 5** and **6** summarizes the crystal lattice parameters, unit cell data, the Miller indices h, k, l, and the data obtained after indexing the powder pattern. The standard deviation observed was within the permissible range.

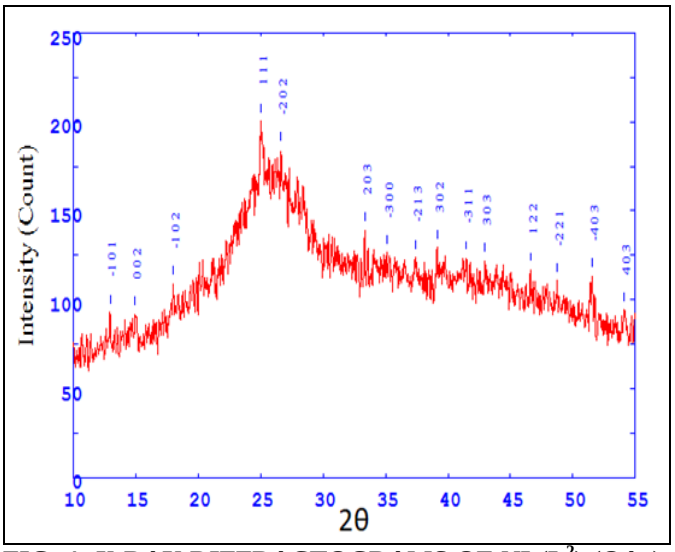


FIG. 4: X-RAY DIFFRACTOGRAMS OF NI (L^2) (OAc). $3H_2O$

TABLE 5: X-RAY DIFFRACTION DATA OF THE Ni(L^2)(OAc).$3H_2O$ METAL COMPLEX

No. of peaks	2θ(Expt.)	2θ(obs)	d(obs)	d(calc.)	Miller indices of planes h,k,l			Intensity
1	12.955	13.219	6.82819	6.69247	-1	0	1	93.10
2	14.960	14.505	5.91722	6.10155	0	0	2	92.09
3	18.003	17.959	4.92322	4.93534	-1	0	2	109.40
4	25.010	24.967	3.55758	3.56359	1	1	1	200.80
5	26.619	26.618	3.34602	3.34624	-2	0	2	184.72
6	33.345	33.139	2.68492	2.70115	2	0	3	139.39
7	35.089	35.103	2.55534	2.55437	-3	0	0	126.57
8	37.387	37.444	2.40339	2.39985	-2	1	3	124.01
9	39.132	39.090	2.30016	2.30249	3	0	2	129.30
10	41.474	41.270	2.17548	2.18578	-3	1	1	123.43
11	42.973	43.008	2.10303	2.10140	3	0	3	122.03
12	46.602	46.354	1.94734	1.95718	1	2	2	116.97
13	48.732	48.685	1.86711	1.86881	-2	2	1	110.78
14	51.518	51.309	1.77250	1.77922	-4	0	3	113.77
15	54.106	54.214	1.69365	1.69053	-4	0	3	94.13

TABLE 6: UNIT CELL DATA AND CRYSTAL LATTICE PARAMETER OF THE Ni(L^2)(OAc).$3H_2O$ METAL COMPLEX

Parameter	Data	Parameter	Data
a(Å)	7.680	Volume (A◦)	404.87
b(Å)	4.320	Space group	P21/n
c(Å)	12.230	Lattice type	P
α(degree)	90	Crystal system	Monoclinic
β (degree)	93.800	Density (obs.)	1.960
γ(degree)	90	Density (calc.)	1.990

Based on the above physicochemical and spectral evidence, we can suggest that the newly synthesized Schiff base metal complexes 1–8 are octahedral structures as described in **Fig. 5**.

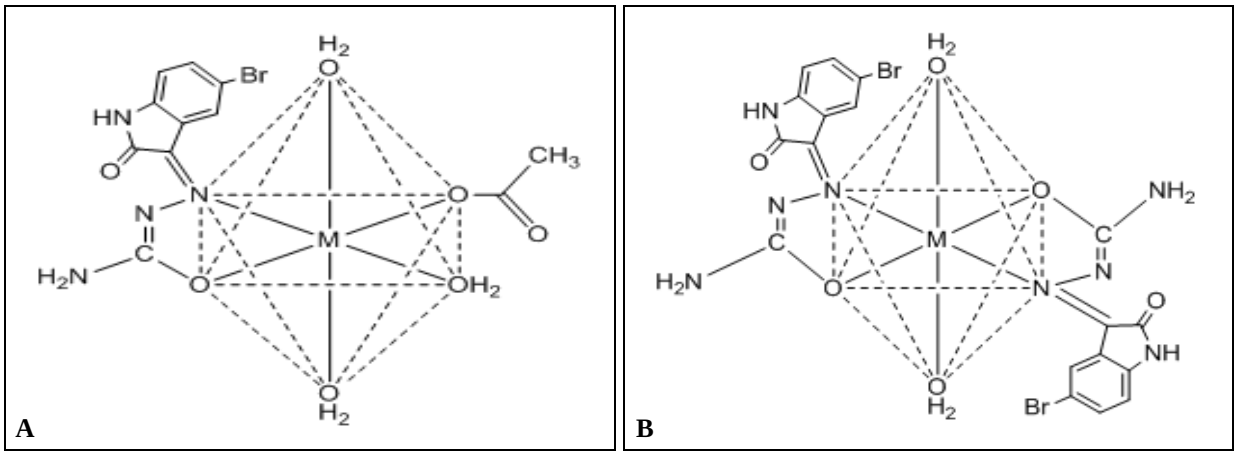


FIG. 5: STRUCTURE OF METAL COMPLEXES WHERE X = O/S; M = Co/Ni (A) = 1:1 V(B) = 1:2

Antibacterial Activity: The biological activity of ligands L^1H, L^2H and their Co (II) and Ni (II) complexes 1–8 against two bacteria (*Staphylococcus aureus* and *Escherichia coli*) has been evaluated. The data were compared with those for the standard drug Streptomycin *i.e.* positive control (for bacteria). All the bacterial strains tested proved to be sensitive both to the ligands and their Co (II) and Ni (II) complexes. The results revealed a significant increase in toxicity of the complexes as compared to their respective ligands **Fig. 6**. The ability of metal complexes to cross the phospholipid cell membrane of bacteria can be explained based on Tweedy's chelation theory and Overtone's concept of cell permeability. On chelation, the polarity of the metal ion is reduced to a significant extent due to which an overlapping between ligand orbitals and the positive charge of metal ion takes place. Further delocalization of π-electrons is increased over the whole chelate ring that leads to an increase in the lipophilicity of the metal complexes. Upon complexation, the lipophilic nature of the central metal ion is also increased, which successively favours permeation through the phospholipid layer so that metal complexes can penetrate the bacterial cell membrane and hence can interact with biomolecules that leads to inhibit the cell growth.

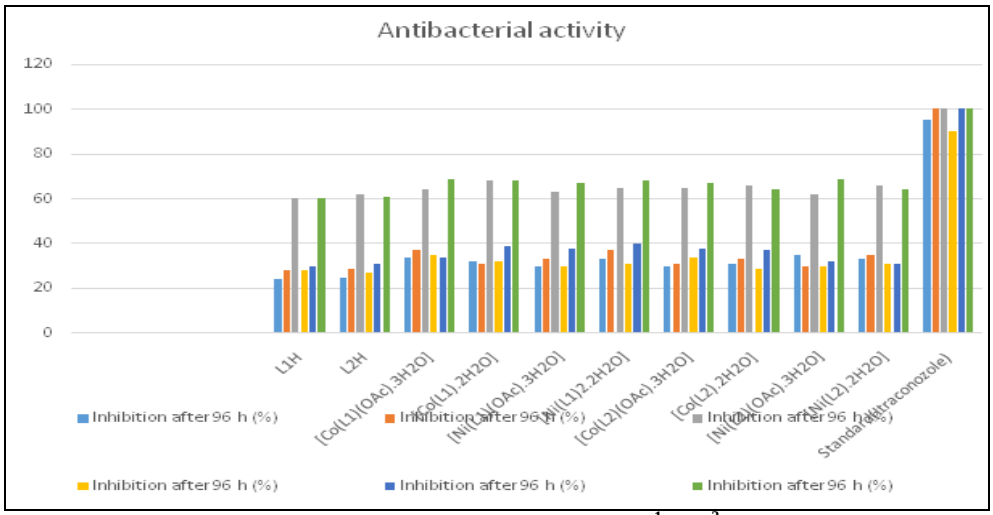


FIG. 6: ANTIBACTERIAL SCREENING OF SCHIFF BASE LIGANDS L^1H, L^2H AND THEIR METAL COMPLEXES

DNA Cleavage Activity: The ligands and metal complexes *i.e.* $Co(L^1)(OAc)\cdot 3H_2O$,$Ni(L^1)(OAc)\cdot 3H_2O$, $Co(L^2)(OAc)\cdot 3H_2O$ and $Ni(L^2)(OAc)\cdot 3H_2O$ were subjected to DNA cleavage activity [Pseudomonas *Aeruginosa* (ATCC-27853)] by gel electrophoresis method [28]. This method was employed to study the efficiency of DNA cleavage by the synthesized Schiff base ligands and their

metal complexes. The difference was observed in banding patterns of lanes 3–8 compared to the control DNA of *Pseudomonas Aeruginosa* (lane 1). The cleavage activities of the metal complexes and ligands are shown in **Fig. 7**. Both the ligands do not exhibit significant cleavage activity (lane 3 & 4). All the metal complexes (lane 5 to 8) showed better DNA cleavage activity than the free ligands. The cleavage activity was greatly enhanced by the incorporation of the metal ion into the respective ligands. Thiosemicarbazone complexes (lane 7 & 8) exhibit better DNA cleavage activity than that of semicarbazone complexes. Thiosemicarbazones based metal complexes are better inhibitors of ribonucleotide reductase and can interrupt DNA synthesis and repair.

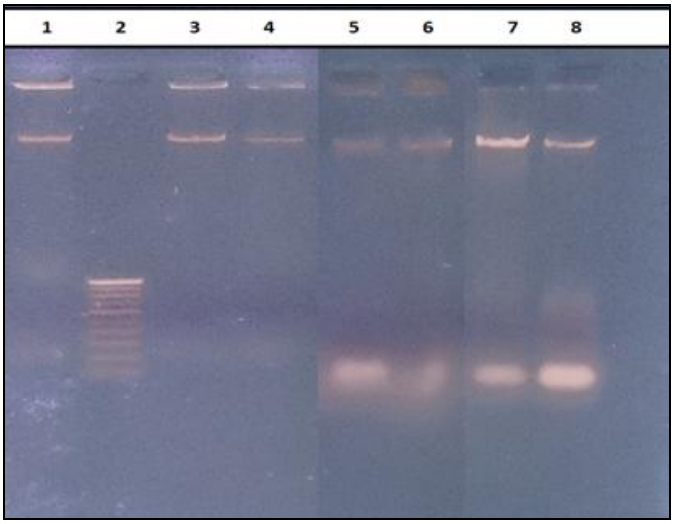


FIG. 7: QUALITATIVE ANALYSIS OF DNA CLEAVAGE BY AGARASE GEL ELECTROPHORESIS OF LIGANDS AND THEIR SCHIFF BASE METAL (II) COMPLEXES. LANE 1- I=UNCLEAVED CONTROL *PSEUDOMONAS AERUGINOSA* GENOMIC DNA, LANE 2- DNA LADDER, LANE 3-4 CLEAVED DNA WITH LIGANDS L^1H AND L^2H, LANE 5 & 6- CLEAVED DNA WITH $Co(L^1)(OAc).3H_2O$ $Ni(L^1)(OAc).3H_2O$ AND LANE 7 & 8- CLEAVED DNA WITH C0 $(L^2)(OAc).3H_2O$

Antioxidant Activity: The generation of free radicals, which is also known as reactive organic species (ROS), in living organisms may bring about millions of extensive cell wall and DNA damage which results in cirrhosis, ageing, mutation, carcinogenesis, atherosclerosis etc in the human system. Transition metal-based antioxidants have been investigated as an effective scavenger of ROS. Antioxidants like H_2O_2, DPPH *etc.* play an essential role in the prevention of tissue damage and do have a capacity to reduce oxidative stress by chelating trace elements or scavenging free radicals and protecting antioxidant defences. The ability of the ligands L^1H, L^2H and their metal complexes i.e. $Co(L^1)(OAc)\cdot 3H_2O$,$Co(L^2)(OAc)\cdot 3H_2O$,$Ni(L^1)(OAc)\cdot 3H_2O$ and $Ni(L^2)(OAc).3H_2O$ to scavenge 1, 1 diphenyl 2- picryl hydrazyl (DPPH) was determined by a method which was developed by Blois (1958) [29] using ascorbic acid as standard **Fig. 8**. DPPH radical is a stable organic free radical with an adsorption band at 517 nm due to its odd electron. The solution appears deep violet, the absorption vanishes as the electron pairs off. The resulting decolorization is stoichiometric with respect to the number of electrons taken up. It loses this adsorption when accepting an electron or a free radical species, which results in a visually noticeable discoloration from purple to yellow. The DPPH assay uses this character to show free radical scavenging activity [30]. The scavenging reaction can be written as;

$$(DPPH) + (H\text{-}A) \longrightarrow DPPH\text{-}H + (A)$$

Fig. 8 shows the comparative effect of Schiff base ligands (L^1H- L^2H) and their metal complexes. It is inferred that Schiff base metal complexes exhibit potent antioxidant activity as compared to free ligands. Results revealed that the compound $Co(L^2)_2.2H_2O$ exhibited the highest antioxidant activity than that of other metal complexes.

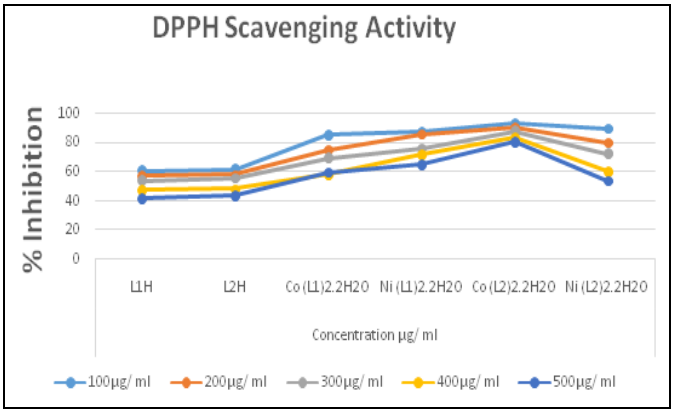


FIG. 8: ANTIOXIDANT ACTIVITY OF LIGANDS AND THEIR SCHIFF BASE METAL (II) COMPLEXES

CONCLUSION: Based on the analytical data and spectral results, an octahedral geometry for the synthesized Cobalt (II) and Nickel (II) compounds has been proposed. The biological screening results of the ligands and their metal complexes show that the complexes are more potent antibacterial agents than the parent ligands due to the chelation. The metal complexes showed a high DNA cleavage

activity as compared to the ligands. The DNA cleavage activity of the Schiff base metal complexes determined on double-stranded *Pseudomonas Aeruginosa* (ATCC-27853) showed that these complexes cleave DNA by an oxidation mechanism. Among the examined compounds Co (II) complexes *i.e.* Co $(L^2)_2.2H_2O$ have exhibited a good scavenging activity, whereas Ni (II) complexes have shown moderate activity. The results of the present research can be useful in the development of conceivable applications in the analytical, biological, and pharmaceutical fields.

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REFERENCES:

1. Çavu¸so˘glu BK, Sa˘glık BN, Osmaniye D, Levent S, Çevik UA, KaradumanAB, Özkay Y and Kaplancıklı ZA: Synthesis and biological evaluation of new thiosemicarbazone derivative Schiff bases as monoamine oxidase inhibitory agents. Molecules 2018; 23: 60.
2. Khajouei MR, Farani AM, Moradi A and Aliabadi A: Synthesis and evaluation of the anticonvulsant activity of (Z)-4-(2- oxoindolin-3-ylideneamino)-N-phenylbenzamide derivatives in mice. Research in Pharmaceutical Sciences 2018; 13(3): 262-72.
3. Khalid S, Sumrra SH and Chohan ZH: Isatin endowed metal chelates as antibacterial and antifungal agents. Sains Malaysiana 2020; 49(8): 1891-1904.
4. Alsalihi EI and Al-Fahdawi AS: Synthesis and antibacterial activity of isatin Schiff base derivative with 3-aminoacetophenone and its Ni(II), Co(II) Transition Metals Complexes. ARO 2108; 6(1): 38-45.
5. Vairalakshmi M, Princess R and Johnson RS: Metal complexes of novel Schiff base containing isatin: characterization, antimicrobial, antioxidant and catalytic activity study. Asi J Pharm Clin Res 2019; 12(8): 206-10.
6. Devi J and Batra N: Synthesis, characterization and antimicrobial activities of mixed ligand transition metal complexes with isatin monohydrazone Schiff base ligands and heterocyclic nitrogen base. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2015; 135: 710-19.
7. Lahari K and Sundararajan R: Isatin- A potent anti-microbial agent, Int J Res Pharm Sci 2019; 10(2): 955-70.
8. Khorshidifard M, Rudbari HA, Delikani ZK, Mirkhani V and Azadbakht R: Synthesis, characterization and X-ray crystal structures of vanadium(IV), cobalt(III), copper(II) and zinc(II) complexes derived from an asymmetric bidentate Schiff-base ligand at ambient temperature. J Mol Struct 2015; 1081: 494-505.
9. Visagaperumal D, Justin EE, Munji H and Chandy V: Isatin Schiff Base-An Overview. Pharma Tutor 2018; 6(5): 38-47.
10. Rao R, Reddy KR and Mahendra KN: Synthesis, characterization, antibacterial, antifungal and anthelmintic activities of a new 5 - nitroisatin Schiff base and its metal complexes. Bulg Chem Commun 2014; 46: 11-17.
11. Hossain MS, Roy PK, Zakaria CM and E-Zahan MK: Selected Schiff base coordination complexes and their microbial application: A review. International Journal of Chemical Studies 2018; 6(1): 19-31.
12. Meeran S, Tajudeen SS, Dusthakeer VNA and Shabeer TK: An insight into the anti-tubercular potential of Schiff bases. JPCBS 2018; 6(3): 158-77.
13. Bulatov E, Sayarova R, Mingaleeva R, Miftakhova R, Gomzikova M, Ignatyev Y, Petukhov A, Davidovich P, Rizvanov A and Barlev NA: Isatin-Schiff base-copper (II) complex induces cell death in p53-positive tumors. Cell Death Discovery 2018; 4: 109.
14. Moradi R, Ziarani GM and Lashgari N: Recent applications of isatin in the synthesis of organic compounds. ARKIVOC 2017; I: 148-201.
15. Abdel-Rahman LH, Abu-Dief AM, Moustafa H and Abdel-Mawgoud AAH: Design and nonlinear optical properties (NLO) using DFT approach of new Cr(III), VO(II), and Ni (II) chelates incorporating tri-dentate imineligand for DNA interaction, antimicrobial,anticancer activities and molecular docking studies. Arabian Journal of Chemistry 2020; 13: 649-70.
16. Aziz T, Ullah A, Ullah R, Haq F, Iqbal M, Khan FU, Jamil MI, Raheel M and Kiran M: Synthesis of isatin and itsderivatives and their applications in biological system. BJSTR 2020; 30(4): 23615-621.
17. Vogel AI: A Textbook of Organic Quantitative Analysis, London, 5th ed., 2004.
18. Makode JT and Aswar AS: Synthesis, characterization, biological and thermal properties of some new Schiff base complexes derived from 2- hydroxyl-5- chloroaceto-phenone and S- methyldithiocarbazate. Indian J Chem 2004; 43A: 2120.
19. Vogel AI: A Textbook of Quantitative Chemical Analysis, London, 6th edition, 2006.
20. Balouiri M, Sadiki M and Ibnsouda SK: Methods for in vitro evaluating antimicrobial activity. J Pharm Anal 2016; 6(2): 71-79.
21. Valgas C, De'Souza SM, Smânia EFA and Jr AS: Screening methods to determine antibacterial activity of natural products. Braz J Microbio 2007; 38: 369-80.
22. Isenberg HD: McFarland Standards- Clinical microbiology procedures handbook, vol. 2, ASM Press, Washington D.C, 5.14.11-5.14.14, second edition, 2004.
23. Sudhasankar S, Vijayachandrasekar M, Natarajan A and Pandian SRK: DNA- Binding and cleavage studies of Mn(ii) and Co(ii) complexes of 1-(2,5- Dioxopyrrolidin-1-Yl)(4-Hydroxy Phenyl)Methyl) Thiourea). IJPSR 2018; 9(2): 509-16.
24. Yang L, Liu H, Xia D and Wang S: Antioxidant properties of camphene-based thiosemicarbazones: Experimental and Theoretical Evaluation, Molecules 2020; 25: 1192.
25. Underhill AE and Billing DE: Calculations of the racah parameter B for nickel (II) and cobalt (II) compounds. Nature 1966; 210: 834-35.
26. Bal M, Ceyhan G, Avar B, Kose M, Kayraldiz A and Kurtoglu M: Synthesis and X-ray powder diffraction, electrochemical, and genotoxic properties of a new azo-Schiff base and its metal complexes. Turk J Chem 2014; 38: 22-241.
27. Camargo HA, Rosas CC, Henao JA and Castellanos NJ: Synthesis and X-ray diffraction data of N1,N2 -di(2-hydroxy) benzylidenbenzene-1,2-di-imine, $C_{20}H_{16}N_2O_2$, Powder Diffraction 2018; 33(1): 66-69.
28. Vamsikrishna N, Kumar MP, Ramesh G, Ganji N, Daravath S and Shivaraj: DNA interactions and biocidal activity of metal complexes of benzothiazole Schiff bases:

synthesis, characterization and validation. J Chem Sci 2017; 129(5): 609-22.
29. Blois MS: Antioxidant determinations by the use of a stable free radical. Nature 1958; 181: 1199-1200.
30. Al-Azawi K, AL-Duhaidahawi DL, Al-Amiery A and Kadhum AAH: Synthesis of Schiff base metal complexes with motivating scavenging potential studies. Free Radicals and Antioxidants 2019; 9(1): 1-4.

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