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SYNTHESIS, SPECTRAL PROPERTIES AND BIOLOGICAL ACTIVITY OF TRIVALENT IRON AND COBALT COMPLEXES OF SCHIFF BASE LIGANDS DERIVED FROM SUBSTITUTED ISATIN AND SULPHADRUGS

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ABSTRACT

The generic formula $[ML_2(H_2O)_2]Cl$ used to create a number of novel iron (III) and cobalt (III) complexes using Schiff bases synthesized from substituted isatin and sulphadrugs, by condensing sulpha medicines like sulphamethazine and sulphadiazine with 5-chloroisatin and 5-bromoisatin. Ligands and compounds have been physically and chemically characterized using elemental, spectroscopic (IR, UV-Vis, PMR) and magnetic examinations. These findings demonstrate that the ligands coordinate with metal ions in a bidentate fashion via phenolic oxygen and imine nitrogen. The complexes exhibit octahedral geometry. Fe(III) complexes are paramagnetic in nature, whereas Co(III) complexes are diamagnetic. Additionally, *in vitro* research on compounds against fungi and bacteria has been done.

KEY WORDS : Isatin, sulphadrug, iron(III), cobalt(III), antifungal, antibacterial activity

INTRODUCTION

Synthetic chemistry is playing an innovative role in manufacture of bioactive compounds (Yakan *et al.,* 2020). Isatin (1H-Indole-2,3-dione) is a favoured scaffold and one of the most significant starting compounds for making polyfunctional heterocyclic derivatives with a variety of activity profiles that are well tolerated in people (Kakkar, 2019). Schiff bases of isatin have been reported to exhibit a range of biological actions, including antifungal (Sridhar *et al*., 2002), antiviral (da Silva *et al*., 2001; Dee Maraes *et al*., 2019), and anti-inflammatory (Brandao *et al*., 2020). Due to their accessibility, variety, and unpredictability, transition metal complexes of Schiff bases are the most extensively researched coordination molecules (Sharma *et al.,* 2005; Sharma *et al*., 2006), since the azomethine linkage (-C=N) is a distinctive group.

Sulphadrug derivatives with isatin were synthesized, characterized and tested for antimicrobial activity (Zahid *et al.,* 2012; Abdulbaset *et al*., 2014; Fatima *et al*., 2015). Incorporation of another group in sulphadrug chain may enhance its resistance towards many bacterial strains and addition of metal through chelation improves the activity of the drugs towards pathogens (Jurca *et al.,* 2017; Weaver *et al*., 2016). The metallic part of complex is responsible for effective binding with DNA, thus damaging the vital genetic material of microbes (Zafar *et al.,* 2021).

MATERIALS AND METHODS

All research grade solvents and metal salts were used without further purification. Isatin derivatives and sulphadrugs used, were purchased from Sigma Aldrich. The electronic spectra of complexes were recorded in DMSO solvent using a UV-visible double-beam spectrophotometer (A lab UV next generation) in the 800-200 nm range. Shimadzu FT-IR spectrometers were used to record the IR spectra of the ligands and their complexes in KBr pellets and Bruker-300 spectrometers were used to record the ^{1}HNMR spectra of the ligands and their complexes in DMSO-d_6. Thin capillaries were used to measure melting points using an ambassador melting point instrument. By employing the calibrant $Hg[Co(SCN)_4]$ and a Gouy's balance magnetic measurements were made.

Synthesis of Ligands

Separately dissolved in ethanol, substituted isatin (5

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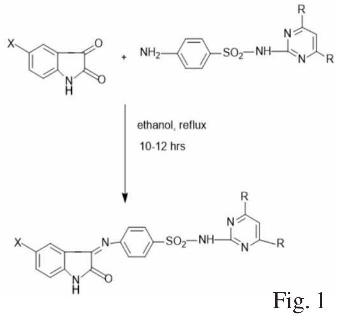
millimole) and sulphadrugs (5 millimole) were mixed after which 2-3 drops of HCl were added. With continuous stirring, the resulting reaction mixture was refluxed for 10 to 12 hours. The combination was kept at room temperature for the night. A coloured precipitate was produced, which was filtered, ether rinsed out, and anhydrous $CaCl_2$ was used to dry it (Sharma *et al.,* 2015). The synthetic route were used to synthesize the ligands in Fig. 1.



Ligand	R	X
L^1	CH_3	Br
L^2	H	Br
L^3	CH_3	Cl
L^4	H	Cl

Fig. 1

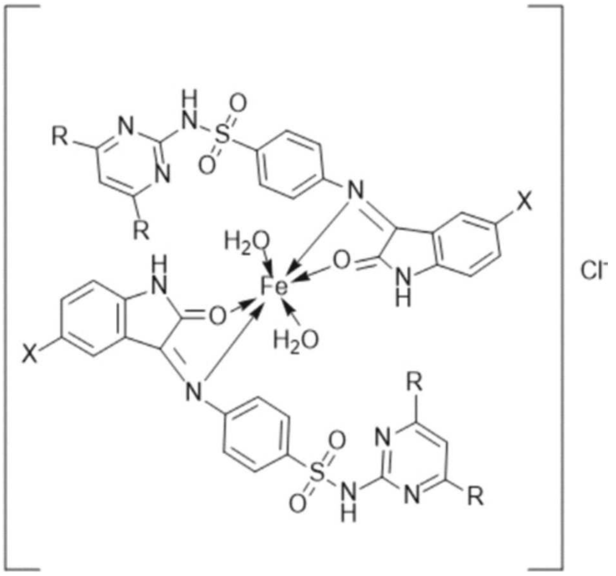


Fig. 2

Table 1: Physical Properties and analytical data of ligands L^1H, L^2H, L^3H, L^4H and their Fe(III) and Co(III) complexes

Compound/ Empirical Formula	Stirring Time (hrs)	Colour	Calc.(found) %							
			C	H	N	S	Cl	Br	O	M
L^1H ($C_{20}H_{16}N_5O_3SBr$)	10-12	brown	49.51 (49.38)	3.19 (3.20)	14.38 (14.40)	6.62 (6.58)	-	16.45 (16.40)	9.91 (9.87)	-
L^2H ($C_{18}H_{12}N_5O_3SBr$)	10-12	yellow	47.25 (44.13)	2.72 (2.61)	16.12 (15.28)	6.90 (6.98)	-	17.90 (17.45)	10.30 (10.47)	-
L^3H ($C_{20}H_{16}N_5O_3SCl$)	10-12	yellowish brown	55.51 (54.31)	3.75 (3.62)	15.91 (15.84)	6.99 (7.24)	8.21 (8.03)	-	10.71 (10.86)	-
L^4H ($C_{18}H_{12}N_5O_3SCl$)	10-12	yellowish brown	52.55 (52.26)	2.99 (2.90)	16.80 (16.92)	7.65 (7.73)	8.65 (8.58)	-	11.51 (11.60)	-
$[FeL^1_2(H_2O)_2]Cl$	12-14	dark brown	43.79 (43.73)	3.12 (3.09)	12.85 (12.75)	5.62 (5.83)	3.53 (3.23)	14.41 (14.57)	11.93 (11.66)	6.52 (5.10)
$[FeL^2_2(H_2O)_2]Cl$	12-14	brown	42.23 (41.47)	2.25 (2.49)	13.82 (13.44)	6.53 (6.14)	4.10 (3.41)	15.92 (15.36)	12.11 (12.28)	6.33 (5.37)
$[FeL^3_2(H_2O)_2]Cl$	12-14	brown	48.11 (47.55)	3.09 (3.36)	14.25 (13.86)	7.52 (6.33)	10.13 (10.54)	-	12.99 (12.67)	5.95 (5.54)
$[FeL^4_2(H_2O)_2]Cl$	12-14	dark brown	45.93 (45.35)	3.53 (2.93)	14.23 (14.69)	6.92 (6.71)	18.09 (17.18)	-	13.11 (13.43)	5.26 (5.87)
$[CoL^1_2(H_2O)_2]Cl$	12-14	dark brown	44.01 (43.61)	2.92 (3.08)	13.15 (12.72)	5.52 (5.81)	3.02 (3.22)	14.19 (14.53)	11.35 (11.63)	4.29 (5.36)
$[CoL^2_2(H_2O)_2]Cl$	12-14	brown	42.21 (41.35)	2.23 (2.48)	13.59 (13.40)	5.98 (6.12)	3.55 (3.39)	14.93 (15.31)	11.92 (12.25)	5.01 (5.64)
$[CoL^3_2(H_2O)_2]Cl$	12-14	reddish brown	48.11 (47.40)	3.95 (3.35)	13.21 (13.82)	6.11 (6.32)	11.00 (10.51)	-	13.09 (12.64)	5.23 (5.82)
$[CoL^4_2(H_2O)_2]Cl$	12-14	reddish brown	46.22 (45.17)	3.02 (2.71)	14.23 (14.64)	6.22 (6.69)	10.95 (11.13)	-	13.93 (13.38)	6.11 (6.17)

Synthesis of complexes with iron(III)

In a 1:2 molar ratio, hydrated iron(III) chloride (0.005 moles) and ligands (0.010 moles) were collected. Separately, both were dissolved in anhydrous ethanol. After mixing, the reaction mixture was then given a few drops of HCl. Refluxing the reaction mixture took 10 to 12 hours. In order to acquire coloured precipitate, the volume of the reaction mixture was decreased to 1/4 by evaporation and then poured into ice cold water. The precipitate was then washed with water, filtered and dried on anhydrous $CaCl_2$ (Sharma *et al.,* 2015).

Synthesis of complexes with cobalt(III)

In a 1:2 molar ratio, $CoCl_2{\cdot}6H_2O$ (0.005 moles) and Ligands (0.010 moles) were taken. Separately, both were dissolved in ethanol. After mixing, the reaction mixture was added 5 ml of 30% H_2O_2 to oxidize Cobalt(II) into Cobalt(III). The reaction mixture was refluxed at pH 6-7 for 10-12 hours. The reaction mixtures volume was then reduced 1/4 by evaporation before being put into ice-cold water to get coloured precipitate. This precipitate, then cleaned with water, filtered and dried on anhydrous $CaCl_2$. Yields ranged from 60 to 65%. A tentative structure of complexes is proposed in Fig. 2.

RESULTS AND DISCUSSION

The condensation of substituted isatin with sulpha pharmaceuticals by refluxing in ethanol has been successful in synthesizing ligands. Then, complexation with hydrated chloride of metal was accomplished by refluxing in ethanol. The physical and analytical information on ligands and their complexes have been described (Table 1). Tetrahydrofuran, dimethylformamide, ethanol and dimethyl sulphoxide are the solvents in which all of the ligands and complexes were soluble.

Table 2: UV-VIS spectra and magnetic moment of complexes

Complexes	Absorption bands (cm^{-1})	Assignments	μ_{eff} (BM)
$[FeL^1_2(H_2O)_2]$ Cl	14500-16990 19350-23100 26500-28800	$^6A_{1g}\rightarrow{}^4T_{1g}$ $^6A_{1g}\rightarrow{}^4T_{2g}$ $^6A_{1g}\rightarrow{}^4A_{1g}$	5.85
$[FeL^2_2(H_2O)_2]$ Cl	do	do	5.74
$[FeL^3_2(H_2O)_2]$ Cl	do	do	5.80
$[FeL^4_2(H_2O)_2]$ Cl	do	do	5.82
$[CoL^1_2(H_2O)_2]$ Cl	15150-15900 21100-21900 23400-23900	$^1A_{1g}\rightarrow{}^3T_{2g}$ $^1A_{1g}\rightarrow{}^1T_{1g}$ $^1A_{1g}\rightarrow{}^1T_{2g}$	Dia.
$[CoL^2_2(H_2O)_2]$ Cl	do	do	Dia.
$[CoL^3_2(H_2O)_2]$ Cl	do	do	Dia.
$[CoL^4_2(H_2O)_2]$ Cl	do	do	Dia.

Magnetic moments

The information on magnetic moments of iron(III) complexes given in Table 2. At ambient temperature, the magnetic moments of iron(III) complexes range from 5.74 to 5.85 B.M., which are projected to be lower values than 5.91 B.M. These near-spin only values indicate a high spin configuration. The complexes of cobalt(III) are, as would be predicted, diamagnetic (low spin, d^6, S=0). This shows that a strong field is produced by an octahedral environment of N and O atoms (Thangadurai & Natarajan, 2000).

Electronic spectral studies

The absoption spectra of all the synthesized complexes have been recorded in the 200-800 nm range in DMSO and their corresponding data are shown in Table 2. In the electronic spectra of iron(III) complexes, weak bands appear at 14,500-16990, 19350-23100 and a strong band appear at 26500-28800 cm^{-1}, which may be attributed to transitions $^6A_{1g}\rightarrow{}^4T_{1g}$, $^6A_{1g}\rightarrow{}^4T_{2g}$, and $^6A_{1g}\rightarrow{}^4A_{1g}$. Although d-d transitions are forbidden in high spin iron(III) complexes, the high intensity band at 26500-28800 cm^{-1} may be attributed to ligand to metal charge transfer (Sharma *et al.*, 2006). The cobalt(III) complexes are diamagnetic at room temperature, and electronic spectra of its complexes show bands at 15150-15900, 21100-21900, 23400-23900 cm^{-1}. These are similar to those, reported for octahedral cobalt(III) complexes (Tripathi *et al.*, 2011) and may be assigned to $^1A_{1g}\rightarrow{}^3T_{2g}$, $^1A_{1g}\rightarrow{}^1T_{1g}$ and $^1A_{1g}\rightarrow{}^1T_{2g}$ transitions respectively.

Infrared spectra

The important stretching vibrations of ligands and their transition metal complexes are reported in Table 3. The IR spectra of ligands show sharp peaks at 1700-1750 and 1575-1598 cm^{-1} for C=O and C=N stretching respectively. The peaks at 3200-3500 cm^{-1} attributed for N-H and O-H stretching. In the spectra of complexes, C=O and C=N stretching shifts to lower side (1650-1700 and 1523-1571 cm^{-1} respectively) which shows involvement of carbonyl oxygen and azomethine nitrogen in complexation. Sharp peaks at 1100-1160 cm^{-1} are attributed to C-SO_2 moiety, 545-590 cm^{-1} for M-O, 420-480 cm^{-1} for M-N stretching. Abroad band near 3400-3600 cm^{-1} are arising from the overlapping of the stretching vibrations of coordinated water with N-H stretching.

Table 3: Infrared spectral bands (cm^{-1}) of the Schiff bases and their complexes

Ligand/Complex	ν (N-H, H2O)	ν (N-H)	ν (C=O)	ν (C=N)	ν (M-O)	ν (M-N)
L^1H	-	3234	1714	1597	-	-
L^2H	-	3240	1745	1580	-	-
L^3H	-	3235	1747	1590	-	-
L^4H	-	3240	1745	1585	-	-
$[FeL^1_2(H_2O)_2]$ Cl	3525-3589	-	1699	1525	572	428
$[FeL^2_2(H_2O)_2]$ Cl	3518-3590	-	1697	1527	580	435
$[FeL^3_2(H_2O)_2]$ Cl	3516-3599	-	1697	1523	574	424
$[FeL^4_2(H_2O)_2]$ Cl	3518-3599	-	1696	1525	578	426
$[CoL^1_2(H_2O)_2]$ Cl	3520-3598	-	1697	1527	584	437
$[CoL^2_2(H_2O)_2]$ Cl	3419-3685	-	1656	1571	575	480
$[CoL^3_2(H_2O)_2]$ Cl	3419-3670	-	1651	1564	588	485
$[CoL^4_2(H_2O)_2]$ Cl	3490-3595	-	1678	1566	580	430

Table 4: Proton magnetic resonance spectral data (δ, ppm) of the Schiff bases

Ligands	δ (SO$_2$-NH)	δ (N-H of isatin)	δ (Ar-H) of isatin	δ (Ar-H) of sulphonamide	δ (Ar-H) of azene ring	δ (CH$_3$) protons
L^1H	4.1	8.0	7.83-8.0	6.6-7.5	6.9-8.4	2.5
L^2H	4.2	8.0	7.24-8.0	6-5-7.6	6.9-8.5	-
L^3H	4.1	8.0	7.56-8.0	6.6-7.5	6.8-8.4	2.6
L^4H	4.2	8.0	7.33-8.0	6.6-7.6	6.8-8.5	-

Proton magnetic resonance spectral studies

The structure of the Schiff base ligands has been established by the use of ^1H NMR spectroscopy. DMSO-d_6 was used to record ^1H NMR spectra. Table 4 lists the ^1H NMR spectra of the ligands. Singlet for N-H of isatin was appeared at δ 8.0, N-H of sulphonamide drug was appeared at δ 4.0, aromatic hydrogens of isatin appeared at δ 7.7-8.1 and aromatic hydrogens of sulphonamide appeared at δ 6.0- 7.3. The aromatic hydrogens of diazine ring of sulphonamide were appeared at δ 7.0-8.5. In complexes of iron and cobalt with ligands L^1-L^4, aromatic hydrogens of sulphonamide experiences downward shift (δ 8.7) which is assumed to be because of complexation of azomethine N with metal.

BIOLOGICAL EVALUATION

Antibacterial and antifungal *in vitro* activities

Using a technique described by Sharma & Srivastava (2005) and Tweedy (1964), the synthesized Schiff bases and complexes were *in vitro* tested for their antibacterial activity against three bacteria- *Bacillus pumilus*, *Escherichia coli*, and *Staphylococcus aureus*as well as two fungi- *Aspergillus niger* and *Candida albicans*. The test chemical was dissolved in 10 ml of DMF solvent at a concentration of 1 mg/ml to create a stock solution. To obtain dilutions of 500 and 1000 gm/l, the stock solution was properly diluted with sterilized distilled water. To create the control for each dilution, 10 ml of solvent were diluted with sterilized distilled water as opposed to the stock solution. In an agar medium, the bacteria were sub cultured (Sharma & Srivastava, 2005). Thornberry (1950) incubated petri plates at 37°C for 24 hours. Gentamycin, a common antibacterial medication, was also tested under comparable circumstances for comparison. The fungus was sub cultured in a medium made of potato dextrose. Fluconazole, a common antifungal medication, was utilized as a benchmark. The inoculated petri dishes were incubated at 37°C for 48 hours. A sterile metallic borer was used to create wells in the agar material. The diameter (mm) of the zone exhibiting full inhibition was used to calculate activity (Table 5). The degree of growth inhibition was compared

Table 5: Antibacterial and Antifungal screening data of ligands and their Fe(III) and Co(III) complexes

Compounds	Antibacterial activity						Antifungal activity			
	Inhibition zone (μgmL^{-1})						Inhibition zone (μgmL^{-1})			
	Bacillus pumilus		*Escherichia coli*		*Staphylococcus aureus*		*A. niger*		*C. albicans*	
	500	1000	500	1000	500	1000	500	1000	500	1000
L^1H	20	24	20	30	20	30	20	25	20	25
L^2H	24	25	25	30	25	30	19	30	30	30
L^3H	22	28	25	25	20	30	21	28	18	28
L^4H	25	35	25	30	20	25	20	25	20	30
$[FeL^1_2(H_2O)_2]$ Cl	22	28	25	35	25	32	22	28	25	28
$[Fe\ L^2_2(H_2O)_2]$ Cl	26	30	28	35	28	35	25	29	28	35
$[Fe\ L^3_2(H_2O)_2]$ Cl	26	35	27	38	30	36	25	40	35	40
$[Fe\ L^4_2(H_2O)_2]$ Cl	30	35	30	38	30	42	30	35	28	30
$[Co\ L^1_2(H_2O)_2]$ Cl	30	40	29	40	29	38	28	30	27	35
$[Co\ L^2_2(H_2O)_2]$ Cl	30	38	30	45	30	40	29	35	30	35
$[Co\ L^3_2(H_2O)_2]$ Cl	35	30	30	35	30	35	28	35	25	40
$[Co\ L^4_2(H_2O)_2]$ Cl	30	35	30	35	35	40	25	38	30	40

to that of common medications. The following formula was used to determine the proportion of the test organism's growth that was inhibited:

$$\text{Inhibition } (\%) = 100 \times C_d - T_d / C_d$$

Where, C_d is the colony diameter of the control and T_d the colony diameter of the treated set. Each set was kept in triplicate.

CONCLUSION

In the present study iron(III) complexes, $[FeL_2^{1-4}(H_2O)_2]Cl$ and cobalt(III) complexes $[CoL_2^{1-4}(H_2O)_2]Cl$ supported by the isatin derived Schiff base ligands L^1, L^2, L^3, L^4 are synthesized. Chemical and Spectral analytical techniques were used for chemical and spectral characterization of ligands L^1, L^2, L^3, L^4 and their corresponding iron(III) and cobalt(III) complexes respectively. Spectral studies showed that metal atom was coordinated via oxygen and nitrogen atoms of bidentate ligand, demonstrating an octahedral geometry.

The efficacy of the synthesized ligand and complexes was studied for their antibacterial properties against *Escherichia coli* and *Staphylococcus aureus*. In addition, antifungal properties against *Aspergillus niger* and *Candida albicans* were determined. It was observed that complexes were more efficient against studied bacterial and fungal strains than free ligands.

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REFERENCES

Abdulbaset, A.E. & Ahmad, M.A. (2014). Preparation, characterization and biological evaluation of Schiff base of some drug substances. *J. Med. Bioeng.*, 3(3): 185-189.

Annapoorani, S. & Krishnan, C., (2013). Synthesis and spectroscopic studies of trinuclear N_4 Schiff base complexes. *I. J. Chem. Tech. Res.,* 5(1): 180-185.

Arulmurugan, S., Helen, P.K. & Venkatraman, B.R. (2010). Biological activities of Schiff base and its complexes: A Review. *Rasayan J. Chem.,* 3(3): 385-410.

Brandao, P., Marques, C., Burke, A.J. & Pineiro, M. (2020). The application of isatin-based multi-component reactions in the quest for new bioactive and drug like molecules. *Eur. J. Med. Chem.,* 211: 113-102.

Da Silva, J.F.M., Garden, S.J. & Pinto, A.C. (2001). The chemistry of isatins; A review from 1975-1999. *J. Braz. Chem. Soc.,* 12(3): 273-324.

De Moraes, G.P.A.T., Pena, L.J. & Leite, A.C.L., (2019). Isatin derivatives and their antiviral properties against arboviruses: A review. *Mini-Rev Med. Chem.,*19: 56-62.

Fatima, A.J.A. (2015). Ca(II) and Au(II) sulfamethoxazole sulfa-drug complexes: Synthesis, spectroscopic and anticancer evaluation studies. *Oriental J. Chem.,* 31(3): 1277-1285.

Gupta, K.C. & Sutar, A.K. (2008). Catalytic activities of Schiff base transition metal complexes. *Coord. Chem. Rev.*, 252(12): 1420-1450.

Ibrahim, H.S., Abou-Seri, S.M. & Abdel-Aziz, H.A., (2016). 3-Hydrazinoindolin-2-one derivatives: Chemical classifcation and investigation of their targets as anticancer agents. *Eur. J. Med. Chem.,* 122: 366-381.

Jurca, T., Eleonora, M., Gratiela, L.V., Eugenia, M.M. & Luminata, F., (2017). Metal complexes of pharmaceutical substances, spectroscopic analyses developments and applications, *Dr. EramSharmin (Ed), Intech.,*123-139.

Kakkar, R., (2019). Isatin and its derivatives: A survey of recent synthesis, reactions, and applications. *Med. Chem. Comm.,* 10(3): 351-368.

Li, W., Zhao, S.J., Gao, F., Lv, Z.S., Tu, J.Y. & Xu, Z., (2018). Synthesis and in vitro anti-tumor, anti-mycobacterial and anti-HIV activities of diethylene-glycol-tethered bis-isatin derivatives. *Chemistry Select,* 3: 10250-10254.

Penthala, N.R., Yerramreddy, T.R., Madadi, N.R. & Crooks, P.A., (2010). Synthesis and in- vitro evaluation of N-alkyl-3-hydroxy-3-(2-imino-3-methyl-5-oxoimidazolidin-4-yl) indolin-2-one analogs as potential anticancer agents. *Bioorg. Med. Chem. Lett.,* 20: 4468-4471.

Sharma, V.K., Srivastava, S. & Srivastava, A., (2005). Transition metal chelates of Schiff bases derived from isatin and amino acids as potential antifungal agents. *J. Appl. Biosci.*, 31(2): 114-121.

Sharma, V.K., Srivastava, S., & Srivastava, A., (2006). Synthetic, structural and antifungal studies of coordination compounds of ruthenium(III), rhodium(III), and iridium(III) with tetradentate Schiff bases. *Polish J. Chem.,* 80: 387-396.

Sharma, V.K., & Rachna (2015). Ruthenium(III) and rhodium(III) complexes with isatin and dithiooxamide coordination Schiff base derivatives: Synthesis, charac-terization and biological activities. *J. Appl. Biosci.,* 41(1): 19-26.

Siraj, I.T. & Ad, H.B., (2018). Synthesis, characterization and anti-microbial activities of Schiff base derived from sulfamethoxazole and isatin and its cobalt(II), copper(II), and zinc(II) complexes. *Du. J. Pure and Appl. Sci*., 4: 426-435.

Sridhar, S., Sarvanan, M., & Ramesh, A., (2001). Synthesis and antibacterial screening of hydrazones, Schiff and manic base of isatin derivatives. *Eur. J. Med. Chem*., 36(7-8): 615-625.

Thangadurai, D. & Natarajan, K., (2000). New ruthenium(III) complexes containing tetradentate Schiff bases antimicrobial activity. *Trans. Met. Chem*., 25(3): 347-351.

Thornberry, H.H. (1950*). Phytopathology*., 40: 419.

Tripathi, N., Shalini & Sharma, V. K., (2011). Synthesis, characterisation and biological aspects of iron(III) and cobalt(III) complexes with Schiff bases derived from substituted mercaptotriazole. *Rev. Roum. Chim.,* 56(3): 189-196.

Tweedy, B.G., (1994). Plants extracts with metal ions as potential antimicrobial agents. *Phytopathol.*, 55: 910-914.

Weaver, G.W., Elsegood, M.R., Tariq, M. & Amina, M., (2016). Synthesis and characterization of new Schiff base transition metal complexes derived from drug together with biological potential. *J. Nuc. Med. and Radiation Therapy,* 7(6): 1-4.

Yakan, H., Bakýr, T.K., Çavuþ, M.S. & Muglu. H., (2020). New β-isatin aldehyde-N, N'-thiocarbohydrazones: Preparation, spectroscopic studies and DFT approach to antioxidant characteristics. *Res Chem. Inter. Med.,* 46: 5417-5440.

Zafar, W., Sumrra, S.H. & Chohan, Z.H., (2021). A review: Pharmacological aspects of metal based 1,2,4-triazole derived Schiff bases. *Eur. J. Med. Chem.,* 222: 113602.

Zahid, H.C., Hazoor, A.S. & Claudiu, T.S., (2012). Synthesis, characterization and biological studies of sulfonamide Schiff bases and some of their metal derivatives, *J. Enz. Inhi. and Med. Chem.,* 27(1): 58-68.