IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

Exploiting the INH Pharmacophore: Synthesis and Study of its Transition Metal Complexes for Biological Applications

Zamzam Taher Omar (Al-Ahdal)[1], Shivaji Jadhav*[2], Rashmi Pathrikar[3], Megha Rai[1]
[1]Department of Chemistry, Dr.Rafiq Zakaria College for Women, Aurangabad, MS, India.
[2]Department of Chemistry, Tarai College Arts and Science, Paithan, Aurangabad, MS, India.
[3]Department of Chemistry, Rajshri Shahu College, Pathri, Aurangabad, MS, India.
Corresponding author mail ID: *dr.shivaji1985@gmail.com

Abstract: *A novel Schiff base ligand incorporating the isoniazid (INH) pharmacophore was synthesized and utilized to prepare a series of paramagnetic transition metal complexes, characterized using spectroscopic techniques (IR, UV-Vis, ^{1}H NMR, ^{13}C NMR). Potentiometric studies revealed the stability constant order: Zn(II) > Co(II) > Ni(II) > Mn(II) > Cu(II). Biological evaluation demonstrated that the synthesized metal complexes exhibited superior antimicrobial and antifungal activity compared to the organic ligand, with the Nickel(II) complex showing promise as an antifungal agent. These findings underscore the synergistic potential of metal coordination in enhancing the pharmacological applications of the INH pharmacophore.*

Keywords: INH pharmacophore, potentiometric complexation, stability constant, antifungal

I. INTRODUCTION

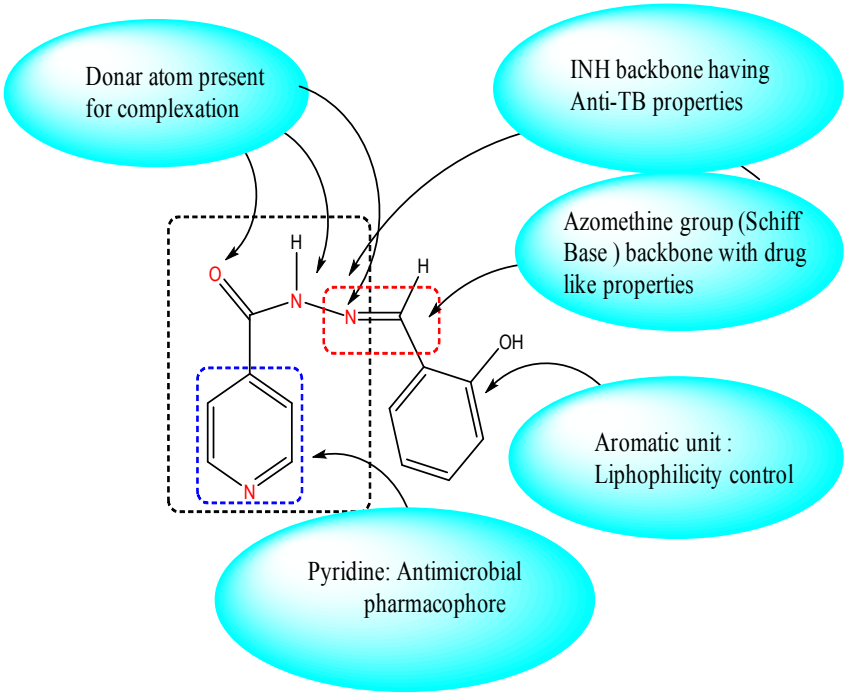
The rational design and synthesis of novel metal complexes incorporating bioactive pharmacophores, such as isoniazid (INH) within a Schiff base scaffold, has garnered significant attention in coordination chemistry [1-4]. Schiff bases, known for their ability to modulate enzyme activity and stabilize metal oxidation states, offer exceptional advantages as complexing ligands due to their structural resemblance to biological molecules, facile synthesis, and structural tunability for targeted bioactivity. Beyond their catalytic applications in organic transformations like ketone reduction [5], Schiff base metal complexes are increasingly recognized for their potential to enhance drug precision, solubility, and catalytic efficiency [5]. The broad pharmacological relevance of organic scaffolds bearing donor groups has been extensively documented [6-9], with Schiff bases and their metal complexes occupying a pivotal role across healthcare, pharmaceuticals, agriculture, and biochemistry. Their diverse therapeutic applications, including antibacterial, anticancer, antifungal, antimalarial, antioxidant, and antiviral activities [10-12], alongside their catalytic utility in reactions like hydrolysis and oxygenation [13-14], underscore their importance. The thermal stability and strong chelating ability of Schiff base complexes [16] are advantageous in various applications, including sensing and catalysis [17-20]. Furthermore, their role in polymerization catalysis [21] and as components in solar cells [22] highlights their broader impact. Understanding the thermodynamics of metal complex formation [23] and their magnetic properties [24] is crucial for elucidating their behavior. Given the substantial potential of Schiff base metal complexes as medicinal agents [25-35], this study focuses on the Synthesis and Bio-evaluation of novel transition metal complexes derived from a new Schiff base incorporating the INH pharmacophore.

Copyright to IJARSCT
www.ijarsct.co.in
DOI: 10.48175/IJARSCT-26511

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

II. MATERIAL AND METHODS

Synthesis of Organic Ligand:



Scheme 1: Synthesized Organic Ligand

In our prior work [36-37], we established a protocol for the efficient synthesis of a series of novel INH-based Schiff base conjugates with potential antimicrobial activity, starting from readily available materials. The organic ligands for this study were synthesized through a straightforward condensation reaction between INH and various substituted aromatic aldehydes, catalyzed by glacial acetic acid in ethanol, yielding the desired products with high efficiency (95%).

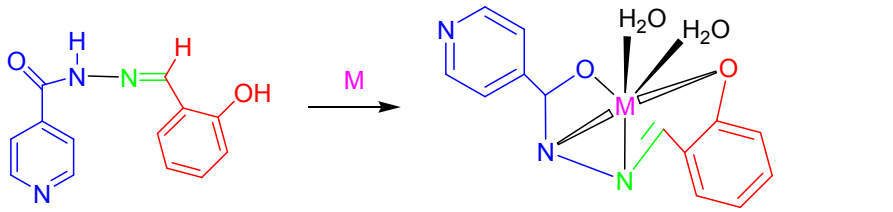
The formation of the INH-incorporated Schiff base (3) was verified by physical data and a suite of spectroscopic techniques: IR, ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectrometry (HRMS). The purity of the synthesized organic ligand was confirmed by a single spot on TLC using EA:DMSO (5:5) as the eluent. Elemental composition was determined via LECO CHNS-932 microanalysis. Spectroscopic characterization involved UV-Vis (190-1100 nm), FT-IR (KBr disc), and NMR (^{1}H at 300 MHz, ^{13}C at 75 or 100 MHz) in $CDCl_3$/DMSO-d_6.

Complexation of biologically active organic ligands with transition metal ions: The pharmacologically active INH-incorporated organic ligand (3), possessing N and O donor atoms for strong metal complex formation, was used for complexation studies. Freshly prepared ligand solutions were crucial to prevent degradation. pH metric titration, a widely accepted and reliable technique due to its ease, accuracy, and robust proton change data, was employed to evaluate the stability constants of the metal complexes. Careful consideration and control of experimental factors, including apparatus, temperature, pH electrode calibration, solution concentrations (ligand, metal ions, acid, alkali, buffer), buffer type, and solvent (freshly prepared double distilled water with pH 6.40-6.80 using KMnO4), were essential for obtaining accurate stability constant values.

Experimental Procedure: Transition metal complexes were synthesized by reacting aqueous metal salt solutions (MnCl2.4H2O, Co(NO3)2.6H2O, Ni(NO3)2.3H2O, Cu(NO3)2.3H2O, and ZnCl2) with the organic ligand in a 1:1 molar ratio in a 30% water/70% ethanol solution (Scheme 3). The pH was adjusted to basic conditions using NH4OH,

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 11, March 2025 Impact Factor: 7.67

and the mixture was refluxed for 4-5 hours, yielding a colored precipitate. After cooling, the solid complex was filtered, washed with distilled water, dried, and weighed. The synthesized complexes were analysed using IR spectroscopy (KBr disc, Bruker FT-IR) to observe changes in functional group frequencies.



organic ligand (3)

Transition metal complexes of schiff base (4)

M^+ : Zn(II), Co(II), Ni(II), Mn(II), Cu(II)

Scheme 3. Synthesis of metal complexes of INH incorporated Schiff.

III. RESULT AND DISCUSSION

Complexation:

Table. 1. Potentiometrically titration data for N-[(E)-(2-Hydroxyphenyl) methylen] isonicotinohydrazid :

N = 0.2 ε^0 **= 0.02N** V_0 **= 50ml**

γ **= 1** T_L^0 **= 0.002N** T_M^0 **= 0.002N**

T = 27 ± 1 **Solvent = 35% Ethanol and 15% water**

Vol. of Alkali Added	pH						
	A	A+L	A+L+Mn+2	A+L+Co^{+2}	A+L+Ni^{+2}	A+L+Cu^{+2}	A+L+Zn^{+2}
0.6	2.13	2.15	2.05	2.07	2.01	2.02	2.05
1.2	2.25	2.22	2.08	2.10	2.07	2.08	2.11
1.8	2.41	2.38	2.14	2.16	2.13	2.14	2.15
2.4	2.61	2.50	2.17	2.22	2.21	2.18	2.20
3	3.05	2.80	2.29	2.27	2.28	2.27	2.24
3.6	10.60	3.95	2.33	2.33	2.47	2.37	2.38
4.2	11.12	7.95	2.44	2.52	3.11	2.58	2.74
4.8	11.30	9.90	2.73	3.01	3.27	3.09	3.18
5.4	11.42	10.18	3.35	3.50	3.87	4.01	3.79
6	11.50	10.70	7.84	7.21	7.56	7.19	7.53
6.6	11.57	10.83	8.32	8.19	8.69	7.86	8.20
7.4	11.64	11.11	8.66	9.10	9.77	9.19	9.13
8	11.70	11.25	9.01	9.57	10.12	9.47	9.63

A representative system of pH-metric titration curve for N-[(E)-(2-Hydroxyphenyl) methylen] isonicotinohydrazid (25d) with transition element Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2}:

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

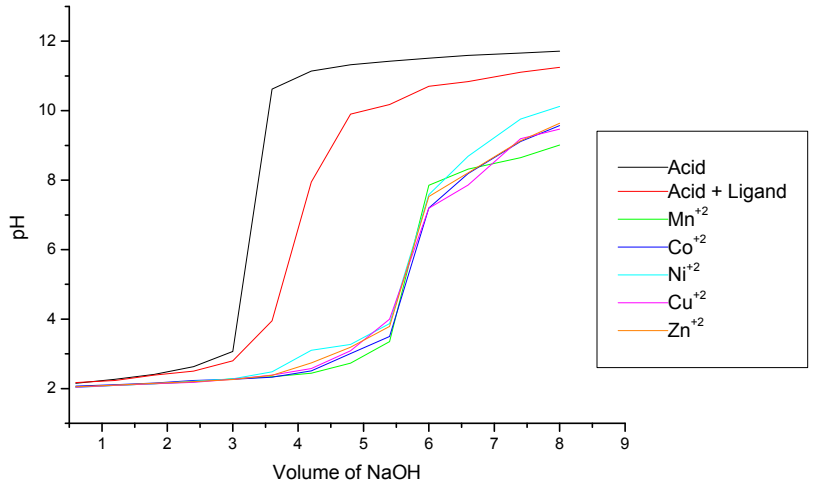


Fig .1: pH-metric titration curve

Table 2: Proton – ligand constant (Protonation constant) of N-[(E)-(2-Hydroxyphenyl) methylen] isonicotinohydrazid:

Ph	V_1	V_2	$\Delta V = V_1 - V_2$	$\bar{n}_A$	pK
2.20	2.57	2.44	0.15	0.675516224	2.518442797
2.40	2.75	2.48	0.2734	0.418972179	2.257988258
2.59	2.99	2.51	0.48	-0.009174312	0.558607315
2.79	2.87	2.55	0.3544	0.259844314	2.345390137
3.00	3.06	2.84	0.2264	0.529402872	3.051137021
3.2	3.42	3.09	0.16	0.668388159	3.504398718
3.4	9.47	3.74	0.108	0.776641768	3.941218779
3.6	10.62	3.92	0.1527	0.684298962	3.935969872
3.8	10.87	6.48	0.25532	0.472195808	3.751649291
4	11.03	7.65	0.388856	0.196237321	3.387653769
4.2	11.14	7.92	0.398496	0.176404363	3.530795287
4.4	11.22	8.87	0.408136	0.156575877	3.668678835

Table 3: Metal-Ligand Stability Constant of N-[(E)-(2-Hydroxyphenyl) methylen] isonicotinohydrazide:

Metal	pK	Stability Constant (logK)
Cu(II)	5.24	4.0703
Ni(II)	5.24	3.9038
Zn(II)	5.24	4.2121
Co(II)	5.24	3.4314
Mn(II)	5.24	3.6133

Physical, elemental and Spectral Interpretation:

N-[(E)-(2-Hydroxyphenyl) methylen]isonicotinohydrazide (Organic Ligand): The novel organic ligand, N-[(E)-(2-Hydroxyphenyl)methylen]isonicotinohydrazid, was synthesized with a 98% yield and a melting point of 245°C. Elemental analysis closely matched the calculated values. The UV-Vis spectrum showed a λmax at 317 nm, indicating a shift to a longer wavelength. Key functional groups were confirmed by FT-IR bands at 3861 cm^{-1} (N-H), 1622 cm^{-1} (C=O), 1679 cm^{-1} (aliphatic C=N), 1389 cm^{-1} (aromatic C=N), 3162 cm^{-1} (C-OH), and 1554 cm^{-1} (Ar-C=C). [38] ^1H NMR and ^{13}C NMR spectra provided detailed structural elucidation, with characteristic signals for the δ 12.268 (s, N-H,

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 11, March 2025 Impact Factor: 7.67

1H)[39] δ11.152(s, OH, 1H) [40-41], δ8.639 (s, Aliphatic-H, 1H), δ8.759-8.751 (d, Pry-H, 2H, J= 3.2Hz), δ7.834-7.830 (d, Pry-H, 2H, J=1.6Hz) δ7.520-7.51 (d, Ar-H, 2H, J=1.6Hz), δ7.501-7.497 (t, 2H, Ar-H, J =1.6 Hz), δ116.86, 118.83, (Benzene C), 121.87, (pry-carbon), 130.03, 132.01(Benzene C), 140.28 (Carbon next to carbonyl carbon), 149.94 (aliphatic N=CH), 150.66 (Pry-Carbon next to N), 158.06 (Carbon next to OH), 161.72 (carbonyl carbon).

FT-IR of transition metal complexes of ligands: In the synthesized transition metal complexes, IR spectroscopy revealed the ligand's coordination mode. The ligand's NH and C=N hydrogen bonds (3646-3444 and 2657-2332 cm^{-1}) were present. The ν(C=N) imine band (1617-1605 cm^{-1}) shifted to lower intensity upon complexation, indicating nitrogen coordination to the metal ion. New bands in the 731-751 cm^{-1} and 670-690 cm^{-1} regions confirmed M-O and M-N bond formation, respectively.

UV-Vis of transition metal complexes of ligands: The UV-Vis spectrum of the organic ligand displayed two absorption bands at 285-287 nm and 328 nm, attributed to π-π* and n-π* electronic transitions within the ligand, respectively. Upon complexation with metal ions, an absorption band was observed in the UV region at 285-287 nm, consistent with a π-π* transition. Additionally, the complexes exhibited absorption bands around 328 nm, which are likely due to charge transfer transitions occurring between the ligand and the metal center (L→M or M→L).

Biological Evaluation: The superior antibacterial action of transition metal complexes compared to their Schiff base ligands is often attributed to **chelation**.[46-49] This binding mode enhances the spread of π-electrons throughout the complex, reduces the metal ion's charge density, and crucially, improves the complex's ability to pass through the fatty cell membranes of bacteria.[50-52] Consequently, Schiff base metal complexes demonstrate a broad spectrum of biological activities, including antiviral, antibacterial, antifungal, antimalarial, antituberculosis, antioxidant, anticancer, anti-HIV, anti-inflammatory, and antipyretic effects.[53-57]

Antimicrobial Evaluation: The antimicrobial evaluation (Table 6) showed that complexation with Cu(II) and Zn(II) significantly enhanced the activity of N-[(E)-(2-Hydroxyphenyl)methylen]isonicotinohydrazid, especially against Gram-negative E. coli. Specifically, these metal complexes outperformed the ligand in their antibacterial effects. The Zn(II) complex displayed broader improvement, showing increased activity against Gram-positive B. megaterium and B. cereus, as well as all tested Gram-negative bacteria. The Cu(II) complex also exhibited enhanced activity against Gram-positive (B. megaterium, B. aureus, B. cereus) and Gram-negative (S. typhi, E. aerogenes, E. coli) strains compared to the ligand. The overall biological evaluation data (Table 6) emphasizes the vital contribution of metal complexation to the ligand's antimicrobial potency, although the tested compounds showed moderate activity when compared to the standard antibiotic tetracycline.

Table 6: MIC value for complex of N-[(E)-(2-Hydroxyphenyl) methylen] isonicotinohydrazid against bacteria, Standard = Pathogens-tetracyclin

Type of bacteria	Species	Ligand (Schiff base)	L+ Mn^{+2}	L+ Ni^{+2}	L+ Cu^{+2}	L+ Zn^{+2}	Standard
Gram positive	B. subtilis	14	R	R	16 mm	10 mm	34 mm
	B.megaterium	12	R	R	9 mm	15 mm	32 mm
	S.aureus	13	R	R	13 mm	10 mm	34 mm
	B.cereus	R	R	R	13 mm	16 mm	33 mm
Gram negative	S. typhi	8	R	R	11 mm	13 mm	31 mm
	E. aerogenes	11	R	R	12 mm	13 mm	33 mm
	P. aerogenosa	14	R	R	13 mm	14 mm	30 mm
	S.abony	12	R	R	R	15 mm	30 mm
	E.Coli	16	R	R	20 mm	16 mm	34 mm
	S.boydii	12	R	R	R	12 mm	30 mm

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

Antifungal Activity: Antifungal testing (Table 7) revealed that the Ni(II) and Zn(II) complexes of N-[(E)-(2-Hydroxyphenyl)methylen]isonicotinohydrazid displayed moderate activity against C. albicans, A. niger, and S. cerevisiae with respect to Standard (Pathogens-nystatin) [58] while other complexes were ineffective. Importantly, the Ni(II) complex showed a remarkable enhancement in its antifungal properties compared to the organic ligand.

Table 7: MIC value for complex of N-[(E)-(2-Hydroxyphenyl)methylen] isonicotinohydrazid against fungi, Standard = Pathogens-nystatin

Fungi	Ligand	L4 + Mn^{+2}	L4 + Ni^{+2}	L4 + Cu^{+2}	L4 + Zn^{+2}	Standard
C. albicans	11	R	14 mm	8 mm	9 mm	30 mm
S. cerevisiae	14	R	14	R	13 mm	29 mm
A. niger	18	R	19 mm	R	13 mm	30 mm

IV. CONCLUSION

Novel transition metal complexes of an INH-based Schiff base were successfully designed, synthesized, and bio-evaluated. Stability constants followed the order Zn(II) > Co(II) > Ni(II) > Mn(II) > Cu(II), indicating their relative stabilities. Antimicrobial tests showed Cu(II) and Zn(II) complexes exhibited superior antibacterial activity, especially against *E. coli*, compared to the ligand. Notably, the Ni(II) complex demonstrated a remarkable improvement in antifungal application. Metal complexation effectively modulated the ligand's bioactivity. The enhanced antibacterial and antifungal properties highlight the potential of these complexes as novel therapeutic candidates. Further research into their mechanisms and in vivo efficacy is crucial for translational applications.

Acknowledgement: Authors are grateful to Dr. Maqdoom Farooqui, Principal, Dr. Rafiq Zakaria College for Women, Aurangabad, MS, India for providing necessary research facilities.

Conflict of interest: Authors state no conflict of interest.

REFERENCES

[1]. Dong-Lai pang., (2019)., Synthesis, characterization and crystal structure of Schiff base nickel(II) complexes with antibacterial activity., Inorganic and Nano-Metal Chemistry., DOI: 10.1080/24701556.2019.1567540.

[2]. Bagila, R. A., Zaragoza, J.P.T., Goldberg, D.P., (2017) Biomimetic reactivity of oxygen derived Manganese and Iron Porphyrinoid complexes., Chem.Rev., 117, 13320-13352. DOI: 10.1021/acs.chemrev.7b00180.

[3]. Sherman, S.E., Xiao, Q., Percec, V., (2017)., Mimicking complex biological membranes and their programmable glycan ligands with dendrimeersomes and glycodendrimersomes., Chem.Rev., 117, 6538-6631., DOI: 10.1021/acs.chemrev.7b00097.

[4]. Jasniewski, A.J., Que, L., (2018)., Dioxygen activation by nonheme diiron enzymes: diverse dioxygen adducts, high valent intermediates, and related model complexes., Chem. Rev. 118, 2554-2592., DOI: 10.1021/acs.chemrev.7b00457.

[5]. Soltani N., Behpour M., Ghoreishi S. M. and Naeimi H., 2010. Corrosion inhibition of mild steel in hydrochloric acid solution by some double Schiff bases, Corrosion Science, 52(4), pp.1351-1361.

[6]. Lapasam, A., Dkhar, L., Poluri, K.M., Kollipara, M.R., (2019), Antimicrobial selectivity of rhuthenium, rhodium, and iridium half sandwitch complexes containing phenyl hydrazone Schiff base ligands towords B.thuringiensis and P.aeruginosa bacteria., Inorg.Chim.Acta., 484, 255-263., DOI:10.1016/j.ica.2018.09.067.

[7]. Patil, S.A., Unki, S.N., Kulkarni,A.D., Naik, V.H., Kamble, U., Badami, S.P., (2011)., Spectroscopic, In Vitro antibacterial, and antifungal studies of Co(II),Ni(II), and Cu(II) complexes with 4-chloro-3-coumarinaldehyde Schiff bases., J.Coord.Chem., 64, 323-336., DOI: 10.1080/00958972.2010.541240.

[8]. Adly,O.M.I., Shebl,M., El-Shafiy,H.F., Khalil, S.M., Taha,A., Mandi,M.A.N., (2017)., Synthesis, spectroscopic characterization, antimicrobial and antitumor studies of mono-, bi-, and tri-,nuclear metal

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

complexes of a new Schiff base ligand derived from O-acetoacetylphenol., J.Mol.Struct., 1150, 507-522., DOI: 10.1016/j.molstruc.2017.08.009.

[9]. Faghih, Z., Neshat,A., Wojtczak,A., Mohammadi, Z., Varestan,S., (2018)., Palladium (II) Complexes based on schiff base ligands derived from Ortho-vanillin: Synthesis , characterization and cytotoxic studies., Inorg.Chim.acta., 471, 404-412., DOI: 10.1016/j.ica.2017.11.025.

[10]. Mahmoud W. H., Deghadi R. G. and Mohamed G. G., (2018), Metal complexes of novel Schiff base derived from iron sandwiched organometallic and 4-nitro-1, 2-phenylenediamine: Synthesis, characterization, DFT studies, antimicrobial activities and molecular docking, Applied Organometallic Chemistry, 32(4), p.e4289.

[11]. Anar M., Özkan E. H., Öğütçü H., Ağar G., Şakıyan İ. and Sarı N., (2016). Useful agents against aflatoxin B1–antibacterial azomethine and Mn(III) complexes involving L-Threonine, L-Serine, and L-Tyrosine. Artificial Cells, Nanomedicine, and Biotechnology, 44(3), pp.853-858.

[12]. Loğoğlu E., Koyuncu E. A., Karaboğa M. N. S. and Sarı N., (2016), Synthesis and a suggestion mechanism on biological evaluation of Amino Acid-Schiff base ligands and Co(II), Cu(II) and Ni(II) Complexes, Gazi University Journal of Science, 29(2), pp.303-307.

[13]. H Chakraborty, N paul, M L Rahman, (1994), Trans. Met. Chem., 19, 524-526.

[14]. Xi Z, Liu W, Cao G, Du W, Huang J, Cai K Guo H., (1987) Chem. Abstr., 106

[15]. R Srekala, K K Yusuff (1999), Chem Abstr. 130.

[16]. Devi N., Sarma K., Rahaman R. and Barman P., (2018), Synthesis of a new series of Ni(II), Cu(II), Co(II) and Pd(II) complexes with an ONS donor Schiff base: crystal structure, DFT study and catalytic investigation of palladium and nickel complexes towards deacylative sulfenylation of active methylenes and regioselective 3-sulfenylation of indoles via thiouronium salt formation, Dalton Transactions, 47(13), pp.4583-4595.

[17]. Salehi M., Faghani F., Kubicki M. and Bayat M., (2018), New complexes of Ni (II) and Cu (II) with tridentate ONO Schiff base ligand: synthesis, crystal structures, electrochemical and theoretical investigation, Journal of the Iranian Chemical Society, 15(10), pp.2229-2240.

[18]. Dutta S. and Biswas P., (2012), Structural, spectroscopic, and magnetic properties of a diphenolate-bridged Fe(III) and Ni(II) complex showing excellent phosphodiester cleavage activity, Polyhedron, 31(1), pp.110-117.

[19]. Wu H., Yang J., Ma J. F., Li, J. Y. and Xie T. F., (2012), Syntheses, structures and photoelectronic properties of a series of tri-and tetra-nuclear metal complexes based on a 36-membered tetraphenol macrocyclic ligand, Polyhedron, 31(1), pp.136-142.

[20]. Samulewski R. B., da Rocha J. C., Stieler R., Lang E. S., Evans D. J., Poneti G., Nascimento O. R., Ribeiro R. R. and Nunes F. S., (2011), Supramolecular assembly of new heteropolymetalic molecules based on tetraiminodiphenolate macrocycle and hexacyanometallate anions magnetostructural and spectroscopic properties, Polyhedron, 30(12), pp.1997-2006.

[21]. Santoro, Orlando, Xin Zhang, and Carl Redshaw., (2020), Synthesis of Biodegradable Polymers: A Review on the Use of Schiff-Base Metal Complexes as Catalysts for the Ring Opening Polymerization (ROP) of Cyclic Esters, Catalysts 10(7), pp. 800.

[22]. Mahadevi, Pichandi, and Shanmugam Sumathi., (2020), Mini review on the performance of Schiff base and their metal complexes as photosensitizers in dye-sensitized solar cells, Synthetic Communications 50(15), pp. 2237-2249.

[23]. Barrett J., (2003), Inorganic chemistry in aqueous solution (Vol. 21), Royal Society of Chemistry.

[24]. Rajbhoj S. W. and Chondhekar T. K., (2000), Systematic Experimental Physical Chemistry, Anjali Publication, Aurangabad, 256.

[25]. Tadele, Kirubel T., and Tilahun W. Tsega., (2019), Schiff bases and their metal complexes as potential anticancer candidates: a review of recent works, Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents) 19(15), pp. 1786-1795.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

[26]. Aslan, Halime Güzin, Senem Akkoç, and Zülbiye Kökbudak, (2020), Anticancer activities of various new metal complexes prepared from a Schiff base on A549 cell line, *Inorganic Chemistry Communications*, 111, pp. 107645.

[27]. Saleem, Muhammad Farrukh, et al., (2021), Synthesis and characterization of some new Schiff base derivatives of gabapentin, and assessment of their antibacterial, antioxidant and anticonvulsant activities., *Tropical Journal of Pharmaceutical Research,* 20(1), pp.145-153.

[28]. El-Gammal, Ola A., et al., (2021), Structural characterization and biological activity of a new metal complexes based of Schiff base, Journal of Molecular Liquids, 330, pp.115522.

[29]. El-Gammal, Ola A., et al. "Structural characterization and biological activity of a new metal complexes based of Schiff base." Journal of Molecular Liquids 330 (2021): 115522.

[30]. Arunadevi, Alagarraj, and Natarajan Raman, (2020), Biological response of Schiff base metal complexes incorporating amino acids–a short review, Journal of Coordination Chemistry, 73(15), pp. 2095-2116.

[31]. Aragón-Muriel, Alberto, et al, (2021), In Vitro Evaluation of the Potential Pharmacological Activity and Molecular Targets of New Benzimidazole-Based Schiff Base Metal Complexes, *Antibiotics,* 10(6), pp. 728.

[32]. Shiju, C., D. Arish, and S. Kumaresan, (2020), Novel water soluble Schiff base metal complexes: Synthesis, characterization, antimicrobial-, DNA cleavage, and anticancer activity, Journal of Molecular Structure, 1221, pp.128770.

[33]. Dhanaraj, Chellaian Justin, and SS Salin Raj, (2020), Synthesis, characterization and biological studies of Schiff base metal complexes derived from 4-aminoantipyrine, acetamide and p-phenylenediamine, *Inorganic Chemistry Communications,* 119, pp. 108087.

[34]. Vamsikrishna, Narendrula, et al., (2020), Synthesis, structural characterization, DNA interaction, antibacterial and cytotoxicity studies of bivalent transition metal complexes of 6-aminobenzothiazole Schiff base, *Inorganic Chemistry Communications,* 113, pp. 107767.

[35]. Rao, N. Nageswara, et al., (2020), Design, synthesis, spectral characterization, DNA binding, photo cleavage and antibacterial studies of transition metal complexes of benzothiazole Schiff base, *Chemical Data Collections,* 27, pp.100368.

[36]. Zamzam T. O., Shivaji Jadhav., & Megha Rai. (2020). Potentiometric and Thermodynamic Studies of (N-[-(4-Chlorophenyl) Methylene] Nicotinohydrazide) and its Transition Metal Complexes. Integrated Ferroelectrics (Tylor & Francis), 2005 (1), 88-94.

[37]. Zamzam T. O., Shivaji Jadhav., Md. Mohsin, Faizaa A.S. & Megha Rai. (2020)., Complexation study of synthesized pharmacological organic ligands with Samarium. Russian journal of inorganic chemistry, Vol. 65(14), 2046-2052.

[38]. El-Sonbati, A.Z., Mahmoud, W.H., Mohamed, G.G., Diab, M.A., Morgan, S.M. and Abbas, S.Y., 2019, Synthesis, characterization of Schiff base metal complexes and their biological investigation. *Applied Organometallic Chemistry*, *33*(9), pp.5048.

[39]. Shebl, M., (2017), Coordination behavior of new bis(tridentate ONO, ONS and ONN) donor hydrazones towards some transition metal ions: Synthesis, spectral, thermal, antimicrobial and antitumor studies, J. Mol. Struct.,1128, pp. 79-93.

[40]. Abdelrhman, E.M. El-Shetary, B.A., Shebl, M., Adly, O.M.I., (2021), Coordinating behavior of hydrazone ligand bearing chromone moiety towards Cu(II) ions: Synthesis, spectral, density functional theory (DFT) calculations, antitumor, and docking studies,Appl. Organometal. Chem.,35, pe. 6183.

[41]. Shebl, M. and Khalil, S.M.E., (2015), Synthesis, spectral, X-ray diffraction, antimicrobial studies, and DNA binding properties of binary and ternary complexes of pentadentate N2O3 carbohydrazone ligands, MonatshChem, 146, pp.15–33.

[42]. Ejidike, I.P. and Ajibade, P.A., (2015), Synthesis, characterization and biological studies of metal (II) complexes of (3E)-3-[(2-{(E)-[1-(2, 4-dihydroxyphenyl) ethylidene] amino} ethyl) imino]-1-phenylbutan-1-one Schiff base. *Molecules*, *20*(6), pp.9788-9802.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 11, March 2025
Impact Factor: 7.67

[43]. Abd El-Razek, S.E., El-Gamasy, S.M., Hassan, M., Abdel-Aziz, M.S. and Nasr, S.M., (2020), Transition metal complexes of a multidentate Schiff base ligand containing guanidine moiety: Synthesis, characterization, anti-cancer effect, and anti-microbial activity. *Journal of Molecular Structure*, *1203*, pp.127381.

[44]. El-Saied, F.A., Salem, T.A., Shakdofa, M.M. and Al-Hakimi, A.N., (2018), Anti-neurotoxic evaluation of synthetic and characterized metal complexes of thiosemicarbazone derivatives. *Applied Organometallic Chemistry*, *32*(4), pp.4215.

[45]. Hossain, M.S., Farzana, K.C., Nayon, U., Kudrat-E-Zahan, M., Laila, A.B. and Haque, M.M., (2019), Synthesis, characterization and antimicrobial activity of metal complexes of N-(4-methoxybenzylidene) isonicotinohydrazone schiff base, *Asian Journal of Chemical Sciences*, *6*(1), pp.1-8.

[46]. Shebl, M., (2009), Synthesis, spectral studies, and antimicrobial activity of binary and ternary Cu(II), Ni(II), and Fe(III) complexes of new hexadentate Schiff bases derived from 4,6-diacetylresorcinol and amino acids., J. Coord. Chem.,62(19), pp.3217-3231.

[47]. Shebl, M., (2016), Mononuclear, homo- and hetero-binuclear complexes of 1-(5-(1-(2-aminophenylimino) ethyl)-2,4-dihydroxyphenyl) ethanone: synthesis, magnetic, spectral, antimicrobial, antioxidant, and antitumor studies, J. Coord. Chem.,69(2), pp.199–214.

[48]. F.A. Cotton, G. Wilkinson., (1986), *Advanced Inorganic Chemistry. A Comprehensive Text*, 4th Edn, pp.761-789.

[49]. Ommenya, F.K., Nyawade, E.A., Andala, D.M. and Kinyua, J., (2020), Synthesis, characterization and antibacterial activity of Schiff base, 4-Chloro-2-{(E)-[(4-fluorophenyl) imino] methyl} phenol metal (II) complexes. *Journal of Chemistry*.

[50]. Neelakantan, M.A., Marriappan, S.S., Dharmaraja, J., Jeyakumar, T. and Muthukumaran, K., (2008), Spectral, XRD, SEM and biological activities of transition metal complexes of polydentate ligands containing thiazole moiety. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *71*(2), pp.628-635.

[51]. Thangadurai, T.D. and Natarajan, K., (2001), Mixed ligand complexes of ruthenium (II) containing α, β-unsaturated-β-ketoaminesand their antibacterial activity. *Transition Metal Chemistry*, *26*(4), pp.500-504.

[52]. Farrell, N., (2002), Biomedical uses and applications of inorganic chemistry. An overview. *Coordination Chemistry Reviews*, *232*(1-2), pp.1-4.

[53]. Kostova, I. and Saso, L., (2013), Advances in research of Schiff-base metal complexes as potent antioxidants. *Current medicinal chemistry*, *20*(36), pp.4609-4632.

[54]. Mohapatra, R.K., Das, P.K., Pradhan, M.K., Maihub, A.A. and El-ajaily, M.M., 2018. Biological aspects of Schiff base–metal complexes derived from benzaldehydes: an overview. *Journal of the Iranian Chemical Society*, *15*(10), pp.2193-2227.

[55]. More, M.S., Joshi, P.G., Mishra, Y.K. and Khanna, P.K., 2019. Metal complexes driven from Schiff bases and semicarbazones for biomedical and allied applications: a review. *Materials Today Chemistry*, *14*, p.100195.

[56]. Uddin, M.N., Ahmed, S.S. and Alam, S.R., (2020), Biomedical applications of Schiff base metal complexes. *Journal of Coordination Chemistry*, *73*(23), pp.3109-3149.

[57]. Hossain, M.S., Farzana, K.C., Nayon, U., Kudrat-E-Zahan, M., Laila, A.B. and Haque, M.M., (2019), Synthesis, characterization and antimicrobial activity of metal complexes of N-(4-methoxybenzylidene) isonicotinohydrazone schiff base. *Asian Journal of Chemical Sciences*, *6*(1), pp.1-8.

[58]. Joseyphus, R.S. and Nair, M.S., (2008), Antibacterial and antifungal studies on some schiff base complexes of zinc (II). *Mycobiology*, *36*(2), pp.93-98