

# Recent Developments in the Antimicrobial Activity of Heterocyclic Compounds

K Vanaja<sup>1</sup> and Dr. Swapnila<sup>2</sup>

Research Scholar, Department of Chemistry<sup>1</sup>

Research Guide, Department of Chemistry<sup>2</sup>

NILM University, Kaithal, Haryana, India

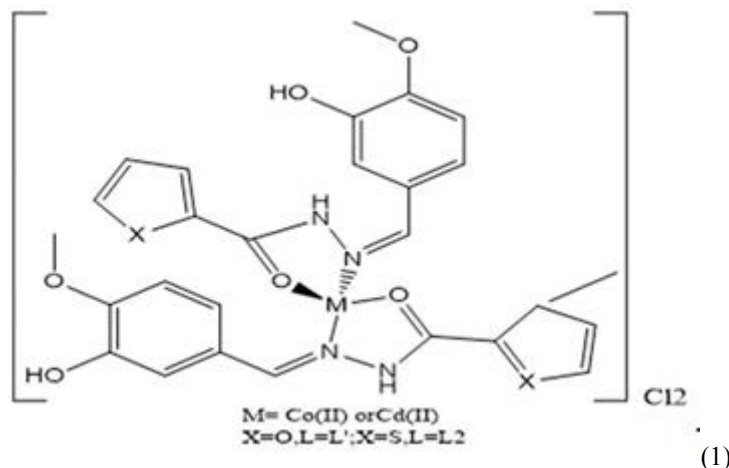
**Abstract:** A vast development in multidrug resistance in antimicrobial action enhances the hunt for high-potential novel medicines. Due to their chelation, fine structural flexibility, and chemotherapeutic characteristics, Schiff base heterocyclic metal complexes containing imine moiety are useful antimicrobials. Schiff base compounds from heterocyclic platforms have been well reviewed.

**Keywords:** hetrocyclic, antimicrobial.

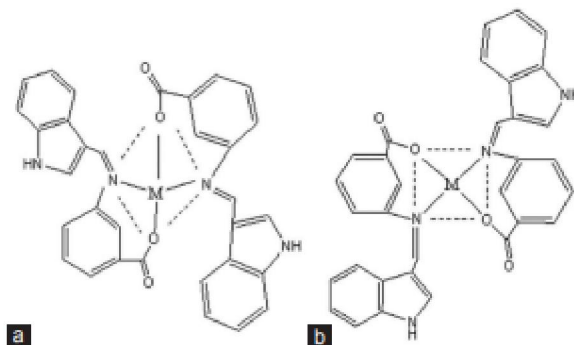
## I. INTRODUCTION

Pharmaceutical research benefited from Schiff base metal complex's expansion as a fine medicine powder. This review covers metal complex anticancer, antifungal, antimalarial, antibacterial, antiproliferative, anti-inflammatory, and antipyretic properties. The metal complex exhibits excellent catalytic and biological activity due to its heat and moisture stabilities. Heterocyclic compounds have high biological activity due to their strong aromaticity with heteroatoms like O, S, and N. Advanced multidrug research causes global antimicrobial resistance. Metal complex drugs made from heterocyclic compounds are excellent. Schiff base metal complex improves heterocyclic compounds' medicinal activity.

In the last decade, Scopus, Pubmed, Google scholar, etc. indexed journal data. More periodicals exist, but we picked sports-related ones. Summary of Schiff base metal complex microbiological activities [1-15].



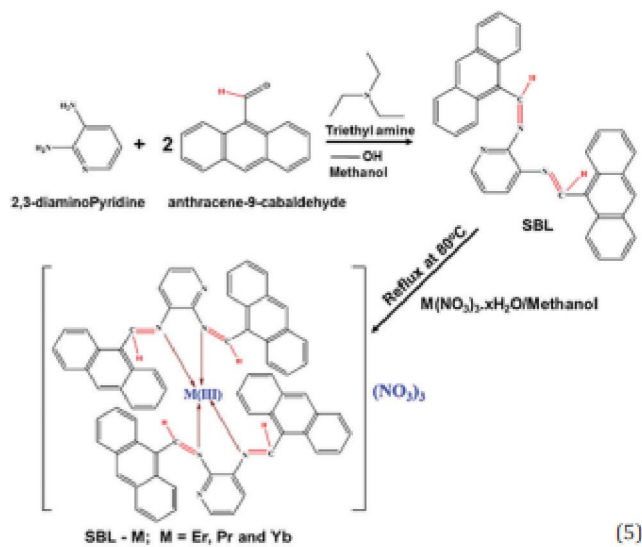
Two new Schiff base ligands from indole-3-carboxaldehyde and m-aminobenzoic acid and their metal complexes from 3rd transition elements Many spectroscopic measurements validated molecular geometry. Co (II) and Ni (II) are tetrahedral, whereas Cu is square planar. By disc diffusion, metal complexes and their ligands are tested for antibacterial and antifungal activities. We employ gel-electro pores. CT DNA assessed ligand nuclear activation. Schiff base metal complex structure: (a) tetrahedral for Co(II), Ni(II), and Zn(II) and (b) square planar for Cu[17].

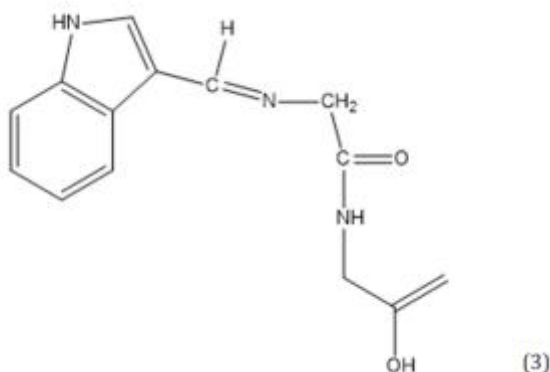


## II. APPLICATIONS OF HETEROCYCLIC COMPOUNDS AS ANTIMICROBIAL AGENT

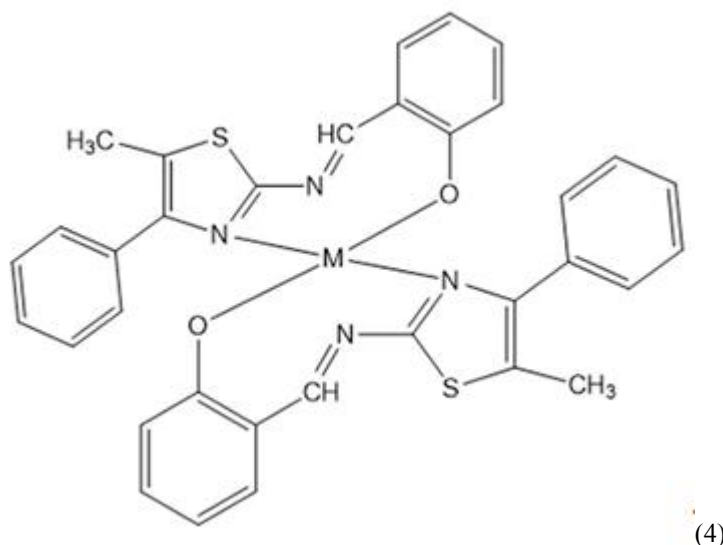
Heterocyclic Schiff base ligands were produced by condensing 3-hydroxy-methoxy benzaldehyde (iso vanillin) with furan-2-carboxylic and thiophene-2-carboxylic Co (II) and Cd metallic-ligand complexes. The metal complex is tetrahedral according to FTIR, UV-Vis, <sup>1</sup>H, <sup>13</sup>C, and magnetic investigations. Gram-negative and Gram-positive bacteria target metal complexes with strong ligands [16].

Pyrrole-ring fused heterocyclic ligands were synthesized from glycylglycine and indole-3-carboxyaldehyde. They have magnetic, electronic, and NMR spectra. Conductance shows metal complexes are 1:1 electrolytes. Peptide nitrogen, carboxylate oxygen, and azomethine nitrogen coordinate metal complexes. Magnetic investigations indicated weak ferromagnetic Co (II) and Cu (II) function paramagnetically. Thermal and IR measurements show water-coordinated metal complexes. TGA/DSC breakdown. XRD showed complicated crystals. The Kirby–Bayer disc diffusion antibacterial activity tested ligands and complexes [18].



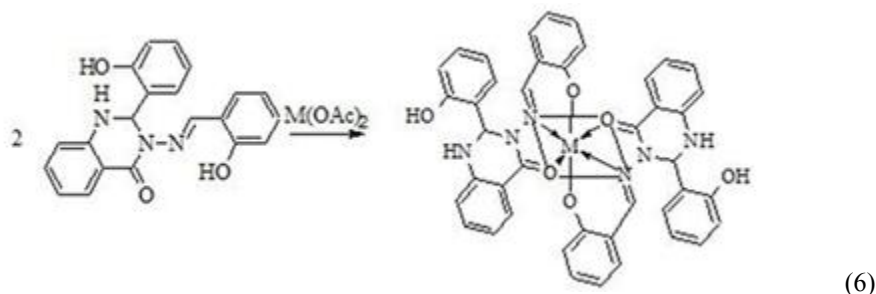


Salicylaldehyde produces a substituted heterocyclic Schiff base ligand with 2-amino-4-phenyl-5-methyl thiazole and transition metal complexes with Co II, Cu II, Ni II, and Zn II. All ligand and metal complex FTIR, NMR, and conductance experiments were done. Zn(II) metal complex inhibited MCF-7, Hep G2, A549, and HCT116 better than doxorubicin [19].

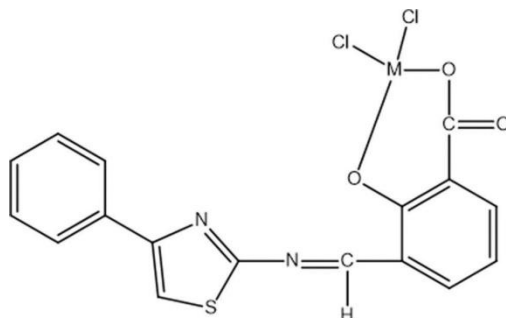


2,6, diamino pyridine and anthracene-9-carbaldehyde produce the Schiff base complex with Pr, Er, and Yb. FTIR indicates a bidentate ligand and two Azo methane-nitrogen coordinations. Metal compound testing against MCF-7 and cervical anticancer cell lines' strong resistance [20].

We synthesized H-HHAQ, an alkaloid-containing heterocyclic Schiff base ligand. Urease inhibition in metal-ligand complexes is investigated. Zn is not enzyme-active like Cu, Co, and Ni. Molecular Cu(II) inhibits more [21].



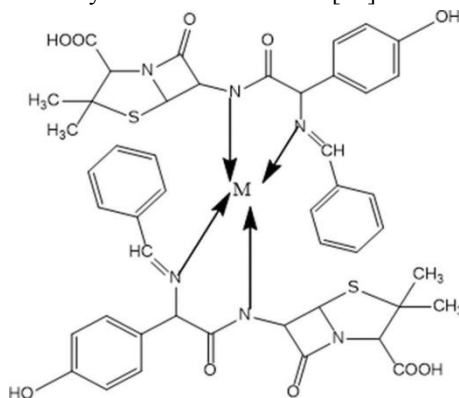
Schiff-based ligand 3-((4-phenylthiazol-2-ylimino) methyl)-2-hydroxybenzoic acid cleaves DNA in vitro with transition metal complexes Cu(II), Co(II), Ni(II), Cd(II), and Zn(II). Elemental, TG/DTA, FTIR, H-NMR, and UV-vis investigations revealed geometry and coordination through bidentate O-O donor. Additionally, Cu, Co, and Zn (II) cleave DNA [22].



M=Cu, Co, Cd, Zn, And Ni

(7) Proposed Structure of the complex

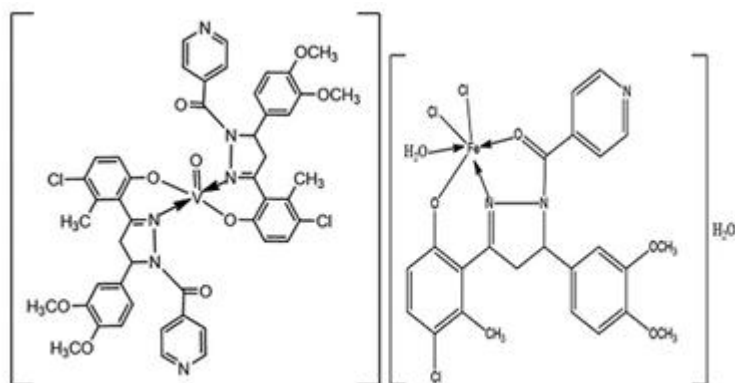
Benzene fused ring system condensation of Schiff-based compounds creates unique Amoxicillin trihydrate and nicotin aldehyde complexes. UV-Vis, SEM, EPR, FTIR, mass spectroscopy, melting point, and conductivity analyzed metal complexes. Powder XRD shows triclinic Cu(II) complexes. A tetrahedral form was suggested for EPR research. The parent medication has strong bacterial activity at two doses in vitro [23].



M=Ni, Cu, Zn

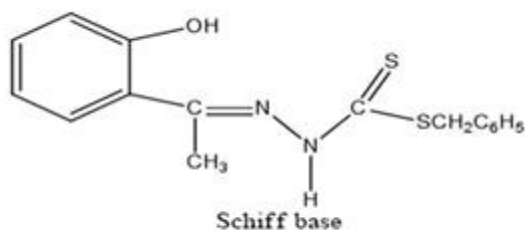
(8)

Latest heterocyclic Schiff-based chemical synthesis from chalcone-3-chloro-6-hydroxy-2-methyl phenyl-3-(3, 4 dimethoxy phenyl) prop-2-en-1-one and isonicotinic hydrazide in ethanol. These compounds are characterized by UV, Mass, FTIR, and molar conductance. IR studies suggest Fe(III) ligand may act as a monobasic tridentate ONO and ON donar against VO (IV). Additional heat stability and complex breakdown studies are available [24].



...(9)

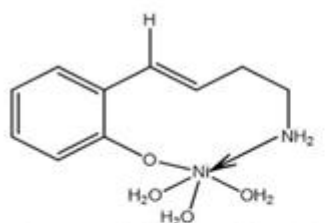
Medical research benefits from metal complex coordination. Synthesis and describe tridentate Schiff base ligands from 2-hydroxyacetophenone and S-benzylidithio carba using magnetic measurements, IR, Electronic Spectra, and molar conductance. Bioactivity depends on molecular geometry. Complex screening shows microbial potential [25].



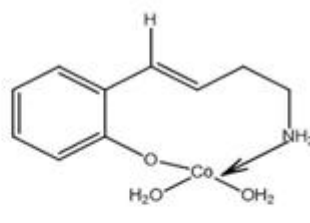
S-benzylthiocarbamate of 2-hydroxyacetophenone

.....(10)

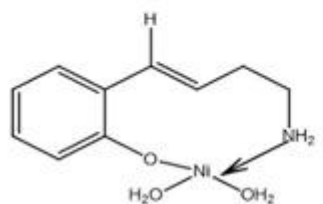
The bactericidal activity of novel Schiff base ligands and their metal complexes was evaluated using ethylenediamine and salicylaldehyde. At various concentrations, Cu inhibited *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumonia*, *Bacillus cereus*, *Salmonella typhi*, and *Staphylococcus aureus* with 9.5, 9.0, and 8.0 mm zones, while Co and Ni had 17, 19, and 22.5 zones. Therefore, these complexes offer effective antibacterial medications for medical research [26].



Structure of Schiff base Ni complex



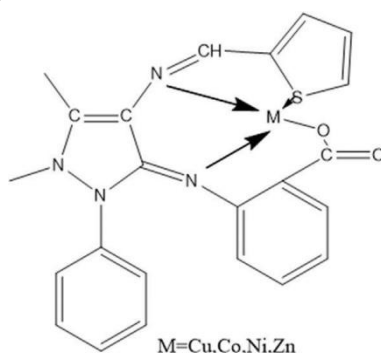
Structure of Schiff base Co complex



Structure of Schiff base Cu complex.

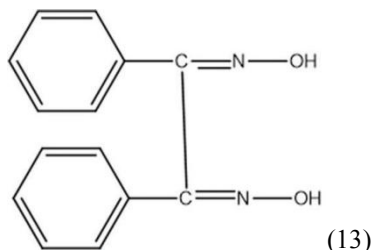
.....(11)

4-AminoAntipyrine and Thioephene-2-carbaldehyde produced Schiff base ligands and Cu(II), Ni(II), and Zn metal complexes. Metal complex structure was identified using spectroscopy. The compound's biological action was explored using ligands and metal complexes [27].

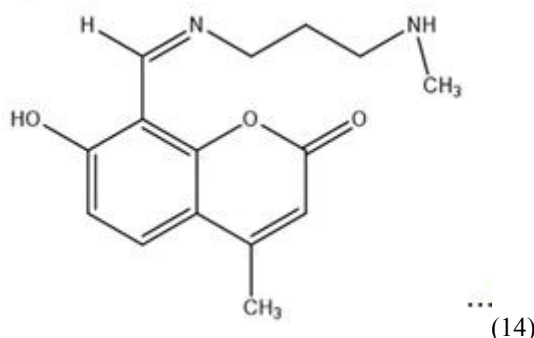


M=Cu,Co,Ni,Zn (12)

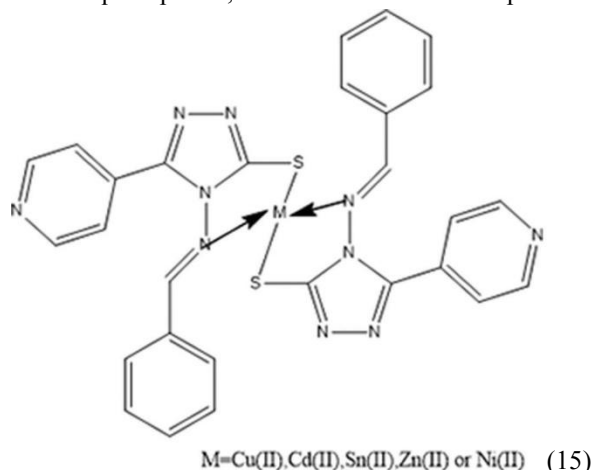
The main and secondary ligands include heterocyclic 2-aminothiazole and 8-hydroxyquinoline containing sulfur and nitrogen and Benzoinoxime. These ligands react with Co (II) and Zn. The major ligand of 1:2:2 metal complexes is oxime. Co (II) metal complexes distort mixed ligands' octahedral geometry, whereas oxime complexes are square planar. Mixed Zn (II) complex ligands contain oximes and deformed octahedral and square planar geometry. Testing complexes for antibacterial activity [28].



Zn(II) complexes from ligands have been synthesized using novel heterocyclic molecules. 8-[(Z)-[3-(N-methylamino) propyl] iminomethyl]-7-hydroxy-4-methyl2H-chromen-2-one, 2-[(E)-{[4-(1H-1,2,4-triazol-1-ylmethyl)phenyl]imino-methyl]phenol (4S)-4-[(E)-(2-hydroxybenzylidene)amino]benzyl-1,3-oxazolidin-2-one. Octahedral Zn(II) complexes were suggested by several spectroscopic techniques. In vitro, Zn(II) complexes outperform Gram-negative and Gram-positive bacteria and fungus such *Candida albicans* and *niger* [29].

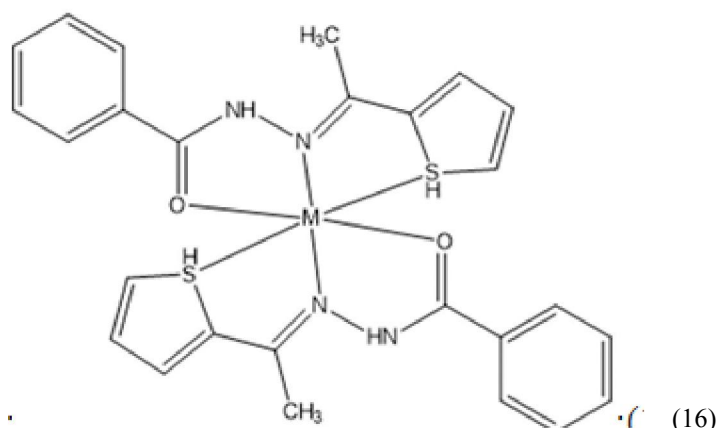


1,2,4 Triazole Schiff base ligands and metal complexes like Cu(II), Cd(II), Sn(II), Zn(II), and Ni(II) are made. Physicochemical investigations show that these compounds' azomethine nitrogen and thiol group S atom coordinate metal complexes. Cu(II) complexes are square planar, whereas other metal complexes are tetrahedral [30].

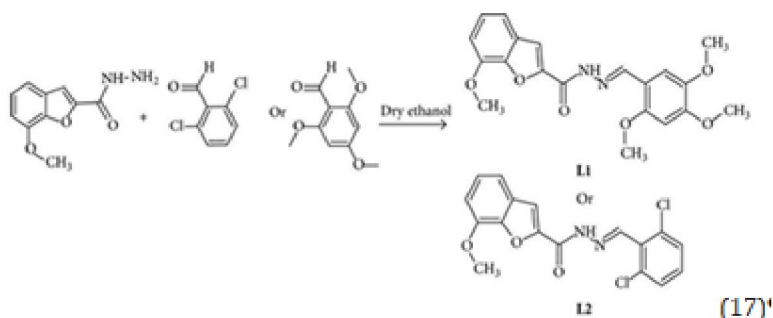


We create metal complexes with triazole Schiff base ligands for Cu(II), Cd(II), Sn(II), Zn(II), and Ni(II). Physicochemical investigations show that these compounds' azomethine nitrogen and thiol group S atom coordinate metal complexes. Other metal complexes are tetrahedral, whereas Cu(II) is square planar [30].

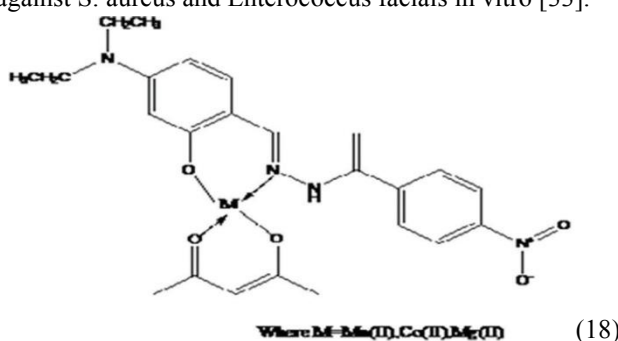




Elements, magnetic moments, and conductance experiments detailed the substituted Benzofuran derivative metal complex. Elemental analysis verifies complex formulations CL-ML n: N1-(2, 4, 5-trimethoxybenzylidene)benzofuran-2-carbohydrazide (L1) or (E)-N1-(2,6 dichlorobenzylidene)-7-methoxy L2. Complexes were tested for antibacterial activity. Metal complexes Co, Cu, and Ni affect all bacteria [32].

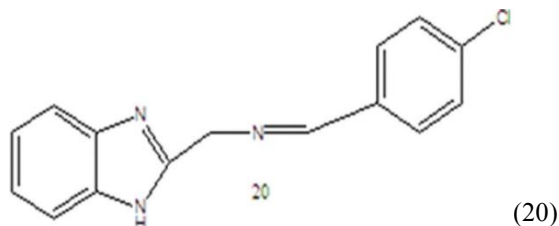


Condensing 4-(diethyl amino)-2-hydroxy benzaldehyde and 4 nitro or 4 methoxy benzo hydrazide yielded the acetylacetonate Schiff base lig Metal complexes were produced using Co(II), Mn(II), and Mg(II). Schiff base bidentate ligands chelate azomethine and phenolic oxygen atoms via nitrogen in FTIR. A metal compound demonstrated promising antibacterial action against *S. aureus* and *Enterococcus facialis* in vitro [33].



Metal complexes from 4-aminoantipyrine, vanillin, and O-anisidine were made. FTIR, NMR, <sup>1</sup>H, and <sup>13</sup>C NMR showed these findings. Metal complexes were antimicrobial-screened. The minimum metal complex inhibitory concentration is more antibacterial than free ligand [34].

(19) Production of a transition metal complex from 2-aminomethylbenzimidazole and 4-chlorobenzaldehyde (1-(1H-benzimidazol)-2H-N-(4-chlorobenzylidene methamine) All metal complexes were shown to be octahedral using <sup>1</sup>H and <sup>13</sup>C NMR, ESR, FTIR, and UV-Vis spectra. Antimicrobial activity against Gram-negative and Gram-positive bacteria was investigated in vitro. The ligand is less active than every metal complex [35].



A. BTSCCH and DMBA metal complexes inhibited five human infections, including *S. aureus*, *B. a K*, and pneumonia. *P. vulgaris*, *E. coli*. Concentrations 0.01%–1%.

Highly bactericidal 10 g/ml metal complex [36].

D. FTIR, electronic Spectra, <sup>1</sup>H and <sup>13</sup>C NMR, DSC, and EDAX electron microscopy evaluated mercury, cadmium, zinc, and lead type M metal chelates. Heat-resistant square planar metal chelates reached 350°C. Cisplatin stopped Gram-positive, Gram-negative, and fungal growth [37].

Using mass spectroscopy, infrared, UV-visible, nuclear magnetic resonance (<sup>1</sup>H and <sup>13</sup>C), and electron spin, Mohamed et al. studied the molar conductance of lornoxicam and 1,10-phenanthroline metal complex. The IR shows neutral bidentate metal ion coordination. Electronic and ESR spectra validated the ternary complex octahedral structure. Check these complexes for bacterial and cancer cell inhibition. Complexes trumped ligands [38].

Ni, Zn, Cd, and Hg(II) transition metal complexes were made from vanillin and 4-aminoantipyrine dihydropyrimidine derivatives. The compounds' UV-vis, <sup>1</sup>H, and <sup>13</sup>C NMRs exhibit ML2. Susceptibility measurements expected a square planar nickel complex, whereas UV-Vis showed a tetrahedral structure. A metallic-ligand complex suppresses microorganisms *in vitro*. Metal complexes are more active than ligands [39]. Hg(II) and Cu(II) perchlorate ions generated two complexes from 2,6-bis(2-aminophenoxy)methylpyridine and 2,2'-bipyridine. 6,6'-dicarboxyaldehyde. All drugs dose-dependently damaged both cell lines. The Hg(II) complex may fight cancer with apoptotic morphology and DNA fragmentation.

H. Salicylaldehyde, 5-methylsalicylaldehyde, ethylene diamine, and diaminomaleonitrile are unsymmetrical Schiff base ligands. The elemental and spectroscopic tests were done. Four copper(II) complex square-planar ESRs. Antimicrobial activity against *S. aureus* in bacteria was tested. Antifungals for *S. aureus*, *B. subtilis*, *K. pneumoniae*. Most metal complexes outperform ligands [41].

J. Schiff base ligands were imidazole-2-carbaldehyde and glycine-glycine. The ligands react with cobalt, copper, and nickel.

K. 1:1 electrolytic molar conductance and Ni<sup>2+</sup> IR demonstrate tetradentate imidazole nitrogen and carboxylate oxygen donors. SEM photos demonstrate complex surface morphology. Fungi and bacteria contain metal complexes. [42].

5-Methyl, 3-Phenyl-1H-Indole-2-Carbohydrazide and 2-hydroxy-1-naphthaldehyde were studied by UV-vis, ESR, thermal, power XRD, conductometry, and magnetic susceptibility. Metal complex screening was antibacterial [43].

New Schiff base compounds with different substituents were tested for their antibacterial capabilities.

### III. CONCLUSION

Schiff base explored versatile antimicrobial activity in the research field. Moreover, metal on complex formation, there *in vitro* antimicrobial activity has increased more when compared to ligands. This review will create new ideas in the field of medicine which helps the scientist to produce more new drugs which are specific in action. In spite of various syntheses in the drug analysis there is still a need to explore new drugs which are useful for future generation.

### REFERENCES

- [1]. Al Mulla A. A review: Biological importance of heterocyclic compounds. *Pharm Chem* 2017;9:141-7.
- [2]. Borad MA, Bhoi MN, Prajapati NP, Patel HD. Review of synthesis of multispiro heterocyclic compounds from isatin. *Int J Rapid Commun Synth Org Chem* 2013;43:1057.
- [3]. Sönmez M, Şekerci M. A new heterocyclic schiff base and its metal complexes. *Synth Reactivity Inorg Metal-Organic Chem* 2010;34:489-502.



- [4]. Kajal A, Bala S, Kamboj S, Sharma N, Saini V. Schiff bases: A versatile pharmacophore. *J Catalysts* 2013;2013:Article ID: 893512, 14.
- [5]. Tobriya SK. Biological applications of schiff base and its metal complexes-a review. *Int J Sci Res (IJSR)* 2014;3:1254-6.
- [6]. Tadele KT. Antioxidant activity of Schiff bases and their metal complexes: A recent review. *J Pharm Med Res* 2017;3:73-7.
- [7]. Parasha RK, Sharma RC, Govind M. Biological activity of some schiff bases and their metal complexes. *Biol Trace Elem Res* 1989;23:145-50.
- [8]. Bernadette SC, Brian D, Denise A, Egana KK, Georgina R. Anticancer and antifungal activity of copper (II) complexes of quinolin-2(1H)-one-derived schiff bases. *Inorg Chim Acta* 2010;363:4048-58.
- [9]. Singh WM, Dash BC. Synthesis of some new Schiff bases containing thiazole and oxazole nuclei and their fungicidal activity. *Pesticides* 1988;22:33-7.
- [10]. Shaikh AA, Raghuvanshi MG, Khurshid I, Molvi K, Nazim S, Ahmed A. Schiff's bases and amides of selected five membered heterocyclic compounds: A review. *J Chem Pharm Res* 2013;5:14-25.
- [11]. Spinu C, Pleniceanu M, Cristian T. Biologically active transition metal chelates with a 2-thiophenecarboxaldehyde derived Schiff base: Synthesis, characterization, and antibacterial properties. *Turk J Chem* 2008;32:487-93.
- [12]. Mehmet G, Mehmet S, Ismet B. Synthesis, characterization, and antimicrobial activity of a new pyrimidine schiff base and its Cu(II), Ni(II), Co(II), Pt(II), and Pd(II) complexes. *Turk J Chem* 2012;36:189-200.
- [13]. Pratibha MS, Vatsala P, Uma V. Biologically active Co (II), Ni (II), Cu (II) and MN(II) complexes of schiff bases derived from vinyl aniline and heterocyclic aldehydes. *Int J Chem Technol Res* 2009;1:225-32.
- [14]. Nazk MA, Shaalanand ND, Sahar S. Synthesis, spectroscopic, thermodynamic and biological activity studies of Schiff base and metal complexes derived from 2-[1h-pyrrol-2-ylimino methyl]-5-phenyl-1,3,4-oxadiazole. *Glob J Sci Front Res B Chem* 2015;15:14-8.
- [15]. Asif NK, Ajay P, Sharad T, Jagannath JK, Lokhande MV. Antibacterial activity of 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol and its some transitional metal ion complexes. *IOSR J Appl Chem* 2014;7:14-20.
- [16]. Abhishek K, Fernandes J, Pankaj K. Synthesis, antimicrobial and anti-inflammatory studies of some novel schiff base derivatives. *Int J Drug Dev Res* 2014;6:165-7.
- [17]. Ahmed RM, Yousif EI, Al-Jeboori MJ. Co(II) and Cd(II) complexes derived from heterocyclic schiff-bases: Synthesis, structural characterization, and biological activity, Hindawi publishing corporation. *Sci World J* 2013;2013:Article ID: 754868, 6.
- [18]. Nair MS, Arish D, Joseyphus RS. Synthesis, characterization, antifungal, antibacterial and DNA cleavage studies of some heterocyclicSchiff base metal complexes. *J Saudi Chem Soc* 2012;16:83-8.
- [19]. Joseyphus RS, Nair MS. Synthesis, characterization and biological studies of some Co(II), Ni(II) and Cu(II) complexes derived from indole-3-carboxaldehyde and glycylglycine as schiff base ligand. *Arabian J Chem* 2010;3:195-204.
- [20]. Abd-Elzaher MM, Labib AA, Mousa HA, Moustafa SA, Ali MM, El- Rashedy AA. Synthesis, anticancer activity and molecular docking study of Schiff base complexes containing thiazole moiety, Beni-Suef university. *J Basic Appl Sci* 2016;5:85-96.
- [21]. Andiappan K, Sanmugam A, Deivanayagam E, Karuppasamy K, Kim HS, Vikraman D, *et al.* *In vitro* cytotoxicity activity of novel schiffbase ligand-lanthanide complexes. *Sci Rep* 2018;8:3054.
- [22]. Ikram M, Rehman S, Subhan F, Akhtar MN, Sinnokrot MO. Synthesis, characterization, thermal degradation and urease inhibitory studies of the new hydrazide based schiff base ligand 2-(2-hydroxyphenyl)-3- {[E)-(2-hydroxyphenyl) methylidene] amino}-2,3- dihydroquinazolin- 4(1H)-one. *Open Chem* 2017;15:308-19.
- [23]. Karabasannavar S, Allolli P, Shaikh IN, Kalshetty MB. Synthesis, characterization and antimicrobial activity of some metal complexes derived from thiazole schiff bases with *in-vitro* cytotoxicity and DNA cleavage studies. *Indian J Pharm Educ Res* 2017;51:490-501.

- [24]. Chaudhary NK, Mishra P. Metal complexes of a novel schiff base based on penicillin: Characterization, molecular modeling, and antibacterial activity study Hindawi. Bioinorg Chem Appl 2017;2017:Article ID: 6927675, 13.
- [25]. Thakare AP, Mandlik PR. Synthesis, spectroscopic and thermal studies of Fe(III) and VO (IV) complexes of heterocyclic schiff base ligand. Indian J Adv Chem Sci 2017;5:318-23.
- [26]. Nasrin D, Alam MA, Hossain MN, Nazimuddin M. Synthesis, characterization and antimicrobial activity of metal complexes of schiff's base derived from S-benzylthiocarbamate with 2-hydroxyacetophenone. Chem J 2013;3:13-9.
- [27]. Sheheryar, Parveen Z, Rahman T, Zeb mMA, Hassan Z, Rehman W. Synthesis and antibacterial activity of schiff base metal complexes. Int J Biosci 2017;10:259-64.
- [28]. Selvi ET, Mahalakshmi S. Synthesis and characterization of heterocyclic schiff base ligand derived from 4-aminantipyridine and thiophene-2- carbaldehyde. Int J Adv Res Dev 2017;2:51-6.
- [29]. Joshi SR, Habib SI. Co (II) and Zn (II) metal complexes of heterocyclic schiff bases: A synthesis, spectral and antimicrobial study. Orient J Chem 2014;30:1343-13.
- [30]. Yamgar RS, Nivid Y, Nalawade S, Mandewale M, Atram RG, Sawant SS, *et al.* Novel zinc(II) complexes of heterocyclic ligands as antimicrobial agents: Synthesis, characterisation, and antimicrobial studies. Bioinorg Chem Appl 2014;2014:276598.
- [31]. Hasan A, Ameer A, Ahmed A, Yousif E. Synthesis and characterization of some transition metal (II) complexes with 1,2,4-triazole schiff base. J Chem Pharm Res 2015;7:531-5.
- [32]. Saadeh SM. Synthesis, characterization and biological properties of Co(II), Ni(II), Cu (II) and Zn (II) complexes with an SNO functionalized ligand. Arabia J Chem 2013;6:191-6.
- [33]. Dikio CW, Ejidike IP, Mtunzi FM, Klink MJ, Dikio ED. Hydrazone schiff bases of acetylacetonate metal Complexes: Synthesis, spectroscopic and biological studies. Int J Pharm Pharm Sci 2017;257-67.
- [34]. Manjula B, Antony SA, Dhanaraj CJ. Synthesis, spectral characterization, and antimicrobial activities of schiff base complexes derived from 4-aminoantipyridine. Spectrosc Lett 2014;47:1-9.
- [35]. Jogi P, Padmaja M, Kumar KP, Gyanakumari C. Studies on DNA cleavage and antimicrobial screening of transition metal complexes of a schiff base derived from 2-(aminomethyl)-benzimidazole and p-chloro benzaldehyde. J Chem Pharm Res 2012;4:1389-97.
- [36]. Dawood ZF, Al-Bustani RR, Taha M. Biological activity of the complexes of Hg(II), Zn(II) and Cd(II) mixed ligands (thiosemicarbazone and azine) Part II. Natl J Chem 2009;36:760-8.
- [37]. Gonerwar NR, Jadhav VB, Jadhav KD, Sakure SS, Killedar AA, Sarawadekar RG. Synthesis, characterisation and antimicrobial activity of bivalent metal (Zn, Cd, Hg, Pb and Ag) chelates of 1,2- naphthoquinone dioxime. IOSR J Pharm 2012;2:25-33.
- [38]. Mahmoud HW, Mohamed GG, El-Dessouky MM. Synthesis, characterization and *in vitro* biological activity of mixed transition metal complexes of lornoxicam with 1, 10-phenanthroline. Int J Electrochem Sci 2014;9:1415-38.
- [39]. Mangaiyarkkarasi P, Arulantony S. DNA cleavage, cytotoxic activities, and antimicrobial studies of some novel schiff base transition metal complexes derived from 4-aminoantipyridine and dihydropyrimidone of vanillin. Int J Curr Pharm Res 2016;8:43-7.
- [40]. Ergene E, Sivas H, Benkl K. Biological activities of Cu (II) and Hg (II) complexes of a heptadentate schiff base ligand. Turk J Biol 2010;34:379-387.
- [41]. Rajasekar M, Sreedaran S, Prabhu R, Narayanan V, Jagadeesh R. Synthesis characterization and antimicrobial activities of Ni (ii) and cu(ii) schiff base complexes. J Coord Chem 2010;63:136-46.