Review Paper:

Heterocyclic Schiff Base and their Metal Complexes: A Review on Antibacterial and Antifungal Activities

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Abstract

Schiff's bases are well-known organic compounds for the synthesis of new "Metal based Drugs" and are synthesized by condensation reaction of different hydrazide or hydrazine with aldehydes or ketones known as imines. Schiff bases and their metal complexes have received remarkable attention among inorganic chemistry researchers due to their unique properties and applications in various fields. They are acting as main source of medicinal compounds displaying anti-inflammatory, antitumor, anticancer, antimalarial, antiviral, anthelmintic and antimicrobial properties in addition to industrial application as food packages, dyes and polymers. Various studies indicate that bioactive compounds having trace amounts of metal ions enhanced their potential to fight against pathogens. Lack of metal ions is causing many diseases including anemia, decrease in growth and cardio-vascular disease amongst children. It is sort out by studying new approaches and new action of mechanism improving the efficiency of the drugs.

Currently, researchers and professional are paying lots of efforts to use Schiff base metal complexes to cure several diseases which are difficult to treat with traditional methods. Metal complexes enhances biological activities and acting as bridge between conventional inorganic and organic compounds. Keeping in mind above mentioned facts, review paper demonstrated mainly on the current pharmacological innovation in the field of synthesis, structural, antimicrobial applications of Schiff bases.

Keywords: Antibacterial activities, Antifungal activities, Schiff base, Metal complexes.

Introduction

Tremendous interest is growing among researchers to do further research in Schiff's base due to their ease of synthesis, metal complexation and in addition, its huge applications for mankind in both developed and developing countries. Chelated Schiff base and their metal complexes are flexible compounds synthesized by the reaction of hydrazide with carbonyl bearing group forming hydrazone[13,26,64,65,57,59,68-72]. Schiff base is synthesized via four different ways: microwave, grinding stone, room temperature and reflux method[59]. Schiff base reactions normally take place with acid/base catalysis or by increasing the temperature. Hugo Schiff was a German chemist who discovered Schiff' base in March 1864. He demonstrated that two moles of aniline react with two moles of an either aliphatic or aromatic aldehyde to give one mole of base and two moles of water illustrated in figure 1.

In addition, it also displays the mechanistic steps involved between benzaldehyde and aniline[68-72]. The above reaction may be reversible due to rapid hydrolysis, it could be overcome by attaching stable aromatic heterocyclic rings. The formation of hydrazone proceeds via following reversible mechanistic steps. First step is nucleophilic attack by the N-atom of primary amine to the carbonyl C-atom of the aldehyde forming an intermediate; second step is intramolecular migration of proton from the ammonium group to the carbinolate group to form carbinolamine and the third step is formation of imine followed by elimination of water.

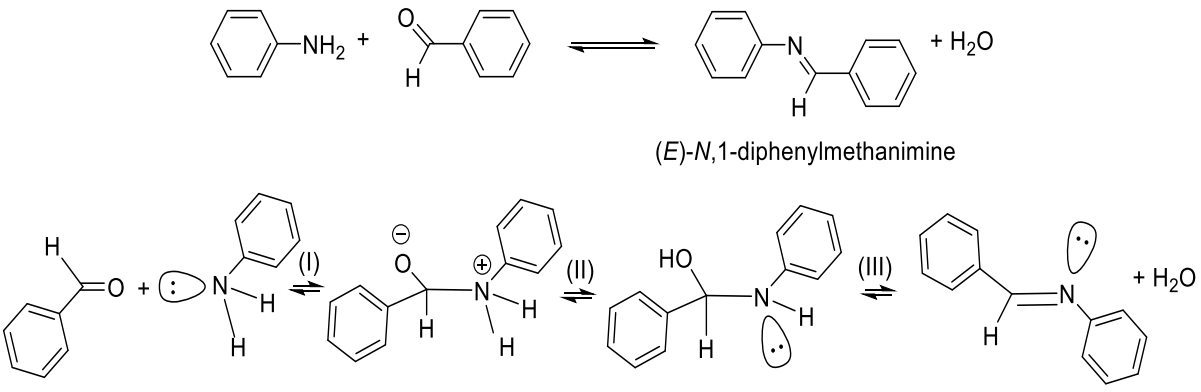


Figure 1: Treatment of aniline with benzaldehyde leading to synthesis of (E)-N, 1-diphenylmethanimine with three reversible mechanistic steps.

Metal ion incorporated within Schiff's base makes huge change in their chemical properties as well as their structural geometry in comparison to simply organic Schiff's base. Various researchers revealed that the presence of –N=C– plays important role to enrich the biological activity of hydrazones and make it a potent pharmaceutical and medicinal agent[78] with a tremendous pharmacological activity including anti-inflammatory[21], antitumor[46,58], anticancer[32,77], antimalarial[73,74], antiviral[12,40], anthelmintic[36], antimicrobial[11,15] properties. Schiff base considered as catalyst in many organic synthesis[47,56].

Due to ease of their strong complexation ability with various d-block ions, it is widely used in analytical chemistry. It is also utilized as a stereo-dynamic chemo-sensor[18,22], in food and beverage industries[35], as dye and pigments[9,45] etc.

Antibacterial and antifungal activity of Schiff's base and their metal complexes: Various research groups are paying huge attention to prepare novel antimicrobial agents to fight microbial resistance. The main objective is to discover new antibiotics to tackle the problem arising due to the lack of effective treatment. It was noticed that the metal complexes display excellent result as compared to ligand against pathogens. Overtone's concept of cell permeability states that the lipophilic compounds are highly soluble in lipid layer of cell membrane causing strong antimicrobial activity. According to chelation theory, the polarity of metal ion will be lowered to a larger extent due to strong overlap of the filled ligand orbital with empty d orbital of metal ion causing delocalization of π-electrons over the chelate ring as a result increasing the lipophilic character in complexes. It can easily penetrate into cell and aggressively kills microorganisms[62,75].

The chromophoric group present in ligand must have OH and azomethine group which binds with active site of the cells via H-bonding thereby enhancing the permeability[51]. The lipophilic metal complexes influenced the process of respiration of cells, followed by blocking proteins synthesis causing the death of pathogens[63]. Gram-negative bacteria comprise of a thin layer of peptidoglycan cell wall, which is surrounded by a lipopolysaccharide outer membrane whereas the Gram-positive bacteria lack the lipopolysaccharide outer membrane but have thicker peptidoglycan layers than Gram negative bacteria[10,43]. Thus, the antimicrobial activity of Schiff's base and their metal complexes varied toward the kinds of bacterial and fungal strains.

Antibacterial and antifungal medicines were used intensively world-wide to cure bacterial and fungal infections, but it can be visualized that most of the bio-organisms have developed tendency to resist to antibiotics, which is of immense threat to mankind. Furthermore, it is important to design and synthesize novel drugs to improve their efficiency by modifying the chemical structures and surrounding functional groups[4,16,27-29]. The molecular structure of compound played a big role in killing the bacterial strains, as the presence of O-atom in the form of OH, N-atom in the form of H-C=N. In addition, chelated metal complexes may interfere in the cell division and hence restrict further growth of the pathogens[5,53,61,79]. The chloride ion coordinated with metal ion also facilitates antimicrobial activity by producing hypochlorous acid which decomposes further to HCl and O_2[14].

The oxygen oxidizes the cellular components and destroyed the microbes. In view of the above-mentioned facts, the metal complexes were screened for their inhibitory effects against the growth of microorganism like bacteria and fungus because it may develop resistance to antibiotics due to biochemical and morphological modifications. The bactericidal and fungicidal activities of compounds were provided which will facilitate researchers and scientists for future research advancement.

Khalil and Mohamed[42] reported novel N^1-(diphenylmethylene)naphthalene-1,8-diamine (1) derived from condensation of benzophenone and 1,8-naphthylenediamine and secondary ligand 1,10-phenanthroline (2), both of them coordinated to metal center forming complexes (3), (4), (5), (6), (7) and (8). *In vitro* antibacterial studies were made towards bacteria *E. coli*, *B. subtilis* and antifungal activities towards *A. flavus* and *C. albicans*.

Results showed that complexes exhibited promising biological activity with the zone of inhibition (in mm) values 9, 13, 25, 17, 11, 30, 30, 28 against *E. coli* 10, 11, 28, 15, 12, 30, 29, 28 against *B. subtilis*, NA, NA, 38, NA, NA 34, 34, 32 against *A. flavus*, NA, NA, 29, NA, NA, 30, 30, 28 against *C. albicans* for (1), (2), (3), (4), (5), (6), (7), and (8) respectively and (1), (2), (4) and (5) were found to be inactive against both fungal strains.

Saranya et al[66] synthesized tetradentate Schiff's base complexes of (9-14) *via* condensation of 2-aminophenol/o-phenylenediamine and terephthaldehyde. The antibacterial studies of compounds were studied against *B. subtilis, P. vulgaris, Klebsiella sp., S. aureus and E. coli*. The complexes (9), (10), (11), (12) and (13) displayed MIC that is % inhibition within 34.48% to 100% towards *S. aureus, E. coli, Proteus sp., Klebsiella sp* and MIC shown by (9), (10), (11), (12), (13) and (14) complexes against *A. niger* as 250 µg/ml, 500 µg/ml, 250 µg/ml, 125 µg/ml, 250 µg/ml and 500 µg/ml respectively. All the data demonstrate that metal complexes were found to kill pathogens drastically killing pathogens.

Diab et al[19] have reported a novel Schiff base ligand, 2,2′-((1E,1′E)- 1,3-phenylenebis(azanylylidene))bis (methanyl ylidene))diphenol (15) from condensation of m-phenylenediamine and 2-hydroxybenzaldehyde followed by synthesis of complexes (16), (17) and (18). Results showed that ligand and some complexes exhibited promising

biological activity with the zone of inhibition (in mm) values 10, 13, 25, 14 against *S. aureus*; 14, 16, 17, 18 against *B. subtilis*; 12, 20, 19, 21 against *Salmonella spp.*; 13, 13, 14, 15 against *E. coli*; 17, 13, 14, 15 against *P. aeruginosa*; 15, 28, 24, 26 against *C. albicans*; 17, 27, 20, 29 against *A. fumigatus*; for (15), (16), (17) and (18) respectively. Screening results highlight that chelated compounds are more potent towards all pathogens as compared to ligand.

Mahmoud et al[50] studied ferrocenyl bases heterocyclic Schiff base ligand, (2-(1-((1-carboxyethyl)imino)ethyl) cyclopenta-2,4-dien-1-yl)(cyclopenta-2,4-dien-1-yl) iron (19) and its mononuclear (20), (21), (22), (23), (24), (25), (26) and (27) complexes and studied their antibacterial activity towards *B. subtilis, S. aureus, E. coli* and *S. typhimurium* and antifungal activities by *A. fumigatus* and *C. albicans,* where gentamycin and ketoconazole act as standard drugs respectively.

Results showed that some complexes exhibited efficient biological activity with the inhibition zone (in mm) NA, NA, NA, 14, 18, 22, 15, 21, NA against *B. subtilis*; NA, NA, NA, NA, 16, 24, 21, 22, 8 against *S. aureus*; NA, NA, NA, 13, 22, 22, 22, 20, NA against *E. Coli*; NA, NA, NA, 12, 20, 21, 16, 14, NA against *S. typhimurium*; NA, NA, 38, NA, NA 34, 34, 32 against *A. fumigatus*; 15, NA, NA, NA, 20, NA, NA, NA, NA against *C. albicans* for (19), (20), (21), (22), (23), (24), (25), (26) and (27) respectively.

The compounds (20) and (27) showed no activity towards all the strains. Ligand (19) was only active against *A. fumigatus*. Ahmed et al[2] reported novel tetradentate Schiff base N,N'-ethylene bis[1-ethyl-6-fl uoro-4-imine-7-(piperazine-1-yl)-quinoline-3-carboxylic acid] (Nor-en) (28) and their complexes Co(II), Ni(II), Cu(II), Zn(II), Y(III), Zr(IV), La(III) and U(VI) (29-36) synthesis. *In vitro* antibacterial studies of complexes were evaluated against *E. coli, S. typhi, S. aureus* and *B. cereus* and antifungal towards *A. niger* and *P. vulpinum.*

The screening results showed inhibition zone areas (in mm) by metal complexes (29): NA, 23.6, 30.3 and 15.6; (30): NA, 32.3, 27 and 12.3; (31): NA, 29.3, 24.6 and 13.6; (32): NA, 28, 32.3 and 14.3; (33): NA, 30.3, 27 and 17; (34): NA, 30.3, 29 and 7; (35): NA, 28.6, 30 and 19.6; and (36): NA, 28.6, 25.6 and 11; against *E. coli, S. typhi, S. aureus* and *B. cereus* respectively.

Results confirmed that complexes were potent towards bacterial strains except *E. coli* and were inactive to the fungal strain. Liu et al[48] prepared Schiff bases from the ferrocenyl chalcone and benzyl dithiocarbazate and its novel bioactive transition metal complexes (37-48). Antimicrobial studies of the synthesized compounds were accomplished against pathogens by disc diffusion method.

Results for Zn(II) complexes (37), (38), (39) exhibited promising biological activity with MIC (M/mL) value 1.349 x 10^{-8}, 2.713 x 10^{-8}, 2.311 x 10^{-8}, 1.893x 10^{-7}, 1.213x 10^{-7}, 2.122 x 10^{-7}, 1.538 x 10^{-8}, 2.301 x 10^{-8}, 1.205 x 10^{-8}, 1.415 x 10^{-8}; 1.268 x 10^{-7}, NA, NA, 1.351 x 10^{-8}, NA, 1.471 x 10^{-8}, 1.891 x 10^{-8}, 1.521 x 10^{-8}, NA, NA; NA, 3.121 x 10^{-7}, 2.871 x 10^{-7}, 3.582 x 10^{-7}, 3.785 x 10^{-7}, 2.531 x 10^{-7}, 1.334 x 10^{-8}, 3.273 x 10^{-8}, 1.312 x 10^{-8}, 1.571 x 10^{-8} against *S. aureus, Streptococcus, Actinomycete, E. coli, P. aeruginosa, C. albicans, A. fumigatus, A. niger, A. flavus* and *S. cerevisiae* respectively.

It showed that MIC values lies in between 1.205 x 10^{-8} and 3.785 x 10^{-7} M, while complex (37) seems to be more active inhibiting the growth of *A. flavus* at 1.205 x 10^{-8} M. Rest of the metal showed variable average inhibitory zone ranging from 12.1 to 23 mm against pathogens. All compounds showed the highest activities against *Streptococcus* and the weakest activities against Actinomycetes.

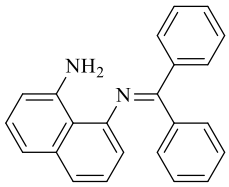
The complexes (37), (38), (39), (43), (45) showed efficient antifungal activities against *A. fumigatus* whereas the complexes (37), (38), (39), (41), (44) showed outstanding fungicidal activities against *A. niger*.

Rest of them were active to *A. flavus*. The compounds (37-39) seem to be more potent with average inhibition values of 21.9, 23 and 21.1 mm against pathogens.

Elshafie et al[25] synthesized Schiff base ligand, GMFX-o-phdn Schiff Base (49) from condensation of gemifloxacin with ortho-phenylenediamine and their complexes and also investigated their antibacterial activity against *E. coli, B. cereus, P. fluorescens and P. aeruginosa*. Antibacterial screening results displayed effective antibacterial activity against *E. coli* and *B. cereus* and low activity against *P. fluorescens* and *P. aeruginosa*.

In particular, the ligand GMFX-o-phdn (49) showed enhanced activity against *E. coli, P. fluorescens* and *P. aeruginosa* and inhibited 34.0, 24.5 and 19.0 mm, inhibition zone areas respectively. The complex (52) was highly active against *E. Coli* with inhibition zone areas 31.0 mm, whereas (52) and (53) showed enhanced activity against *B. cereus* with inhibition zone areas 39.5 and 38.5 mm respectively.

The antifungal studies was performed against fungal strains *M. fructicola, A. flavus, P. italicum and B. cinerea* where cycloheximide was used as standard. Mycelium Growth inhibition percentage against *M. fructicola, A. flavus, P. italicum and B. cinerea,* for ligand GMFX-o-phdn at concentration 1000 μg/ml, NA, 16.1, 38.9 and 20 %; respectively whereas mycelium growth Inhibition percentage against *M. fructicola, A. flavus, P. italicum and B. cinerea* for complexes was (concentration 1000 μg/ml) (50): (NA, 22.7, 52.9 and 43.9 %); (51): (32.6, 44.4, NA and 38.3 %); (52): (NA, 15.8, 42.1 and 23.2 %) and finally for (53) (NA, 16.7, NA and 21.8 %); respectively.



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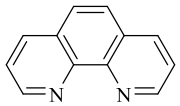

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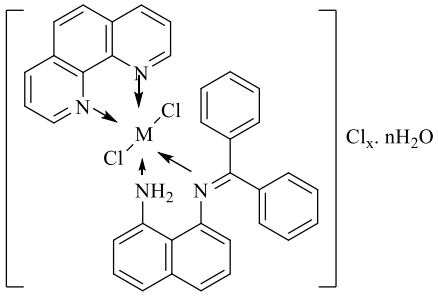
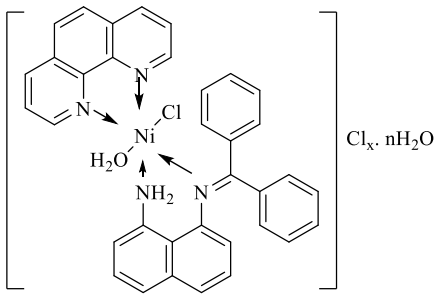


Where M = Mn (II), Zn(II), x = 0, n = 1 **(3-4)**
M = La(III), Er(III) and Yb(III); x = 1, n = 2 **(6,7, 8)**



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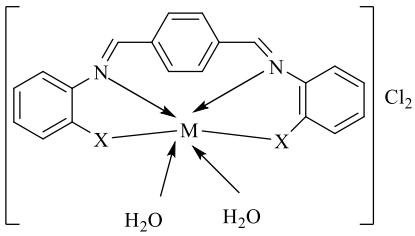
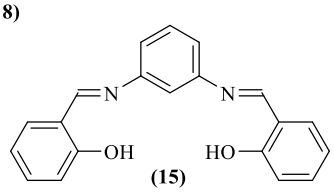


(Where X = OH then M = Cu(II), Co(II) and Ni(II) **(9-11)**;
X = NH_2 then M = Cu(II), Co(II) and Ni(II) **(12-14)**



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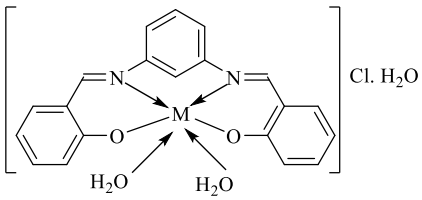
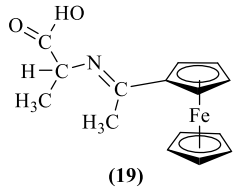


M = La(III), Er(III) and Yb(III) **(16-18)**



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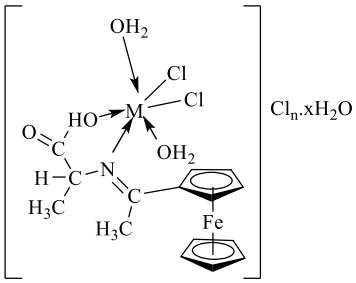
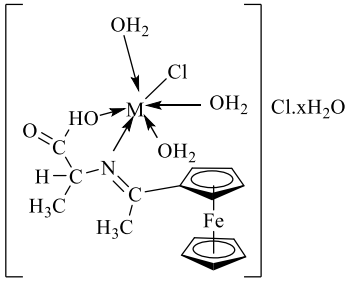
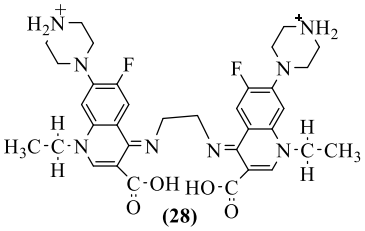




M = Cr(III): n = 1, x = 2; **(20);** Mn(II): n = 0, x = 4; **(21)**
Fe(III): n = 1, x = 3; **(22);** Co(II): n = 0, x = 3; **(23)**
Zn(III): n = 0, x = 5; **(24);** Cd(II): n = 0, x = 2; **(25)**

(M = Cu(II) then x = 3; **(26)**
M= Ni(II) then x = 1); **(27)**



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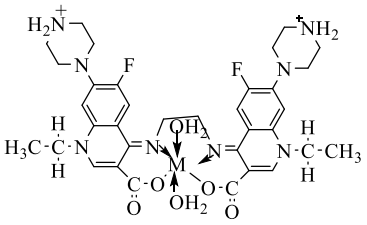
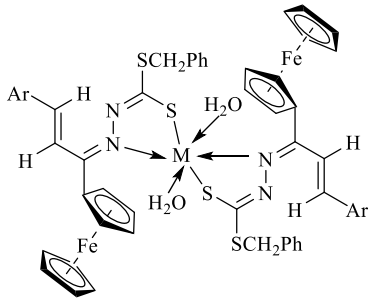
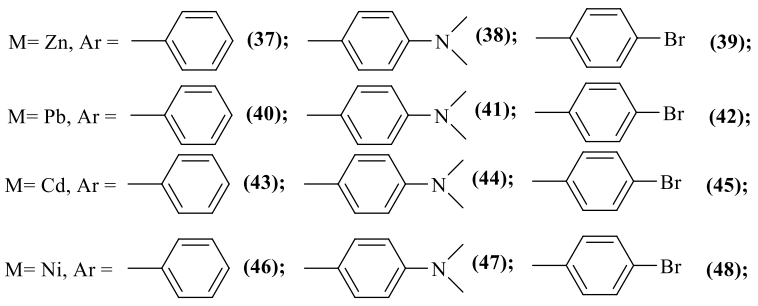


M = Co(II), Ni(II), Cu(II), Zn(II),
Zr(IV) as Zr=O with only one H_2O coordination,
Y(III), La(III), and U(VI) as O=U=O
no H_2O coordination **(29-36)**





M= Zn, Ar = **(37);** **(38);** **(39);**
M= Pb, Ar = **(40);** **(41);** **(42);**
M= Cd, Ar = **(43);** **(44);** **(45);**
M= Ni, Ar = **(46);** **(47);** **(48);**

The screening results suggest that the GMFX-o-phelin ligand was effective against all the fungal strains except *M. fructicola*, whereas amongst the metal complexes, only (51) showed exceptionally good antifungal activity against *M. fructicola* and rest of them were inactive. Abu-Yamin et al[1] investigated a new Schiff base, (1E,2E)-N-(6-ethoxybenzo[d]thiazol-2-yl)-3-(furan-2-yl)prop-2-en-1-imine (54) from the thermal condensation of 3-(2-Furyl)acrolein with 2-Amino-6-ethoxybenzothiazole and its lanthanide complexes of (55), (56) and (57). Screening data of ligand and some complexes exhibited promising biological activity with the inhibition zone area (in mm) values 15.17, 24.01, 14.20, 18.07 against *S. aureus*; 20.10, 26.02, 18.10, 20.80 against *B. subtilis*; 18.17, 29.90, 17.10, 22.60 against *E. coli*; 16.97, 25, 14, 18.60 against *P. vulgaris*; 22.20, 17.01, 19, 23.13 against *A. fumigatus*; 20.10, 20.03, 17.97, 18.78 against *C. albicans* for (54), (55), (56) and (57) respectively.

All the tested ligand and metal complexes showed reasonable activity against pathogenic bacteria, whereas complex (55) showed greater activity and the free ligand (54) showed the strongest activity compared to the standard drug against *A. fumigatus* and *C. albicans*. The screening results of antifungal activity of the metal complexes (55), (56) and (57) seem to surpass than Ketoconazole standard drugs against *A. fumigatus* but almost matching against *C. albicans*. Ahmed et al[3] investigated the antibacterial properties of Schiff bases ligand (58) synthesized by condensation of 4,6-dihydroxy-1,3-phenylenediethanone with ethane-1,2-diylbis(oxy)diethanamine and their metal complexes (59), (60), (61), (62), (63), (64), (65) and (66).

In vitro screening results showed that some of metal complexes displayed better biological activity compared to standard drug with the zone of inhibition (in mm) values for (59): (0, 9, 0, 9, NA, NA); (60): (10, 10, 10, 10, NA, NA); (61): (NA, NA, NA, NA, NA, NA); (62): (22, 21, 22, 22, NA, 21); (63): (13, 12, 13, 12, NA, NA); (64): (11, 11, 10, 10, NA, NA); (65): (18, 24, 19, 20, NA, 11); (66): (19, 18, 18, 19, 27, 15) against *B. subtilis*, *S. aureus*, *E. coli*, *P. aeruginosa*, *A. flavus and C. albicans* respectively whereas, ligand (58) was inactive against bacterial and fungal strain. In case of (62), (65) and (66), the increase in activity may be due to chelation. Mohamed et al[52] reported the antibacterial properties of tridentate (2-(1-((8-aminonaphthalen-1-yl) imino)ethyl)cyclopenta-2,4-dien-1-yl) (L) (67), from condensation reaction between isatin drug and 2,6-diaminopyridine and their metal complexes (68), (69), (70), (71), (72), (73), (74) and (75).

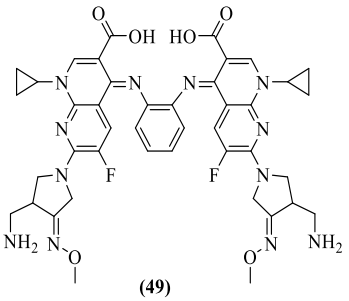
In vitro antibacterial studies of ligand (67) and its complexes (68-75) were performed against *S. aureus*, *B. subtilis*, *Salmonella species*, *E. coli* with reference to Amikacin as standard antibiotic. The compounds inhibited with inhibition zone areas (value in mm) for (68): (10, 12, 12, 10, 9, NA); (69): (10, 9, 13, 11, 13, NA); (70): (11, 9, 11, 11, 11, NA); (71): (10, 13, 13, 11, 11, NA); (72): (10, 0, 13, 16, 14, NA); (73): (11, 11, 11, 11, 10, NA); (74): (0, 0, 12, 14, 14, NA); and (75): (9, 6, 7, 6, 12, NA) against *S. aureus*, *B. subtilis*, *Salmonella species*, *Escherichia coli*, *C. albicans* and *A. fumigatus* respectively. The screening results of compounds (68-75) reported significant antifungal activity against *C. albicans*, both of them exhibiting the strongest activity surpassing the standard drug Ketoconazole, whereas all the compounds (68-75) were inactive against the fungus *A. fumigates*.

El-Gammal et al[23] investigated a new Schiff base hydrazone ligand (HL), from the condensation of salicylaldehyde and 4-(3-cyano-4,6-dimethylpyridin-2-ylamino)benzohydrazide (76) and their metal complexes (77), (78) and (79). Screening results with reference to gentamycin and ketoconazole standard drug showed that complexes (78-79) exhibited promising biological activity with the inhibition zone area (in mm) values 18, 14, 12 against *S. aureus*; 10, 12, NA against *E. coli*; NA, NA, NA against *C. albicans*; for (77), (78) and (79) respectively. The ligand (76) was inactive against tested pathogens and metal complexes (77), (78) and (79) showed no activity against *C. albicans*.

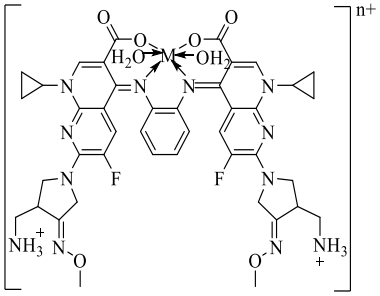
Satheesh et al[67] synthesized a new Schiff base hydrazone ligand L^1H (80) and L^2H (81), from the condensation of 2-hydroxynaphthaldehyde with 2,3-dimethoxyaniline and 2-(3,4-dimethoxyphenyl)ethan-1-amine respectively and their synthesized metal complexes such as $[Zn(L^1)_2]$ (82), $[Cu(L^1)_2]$ (83) $[Zn(L^2)_2]$ (84) and $[Cu(L^2)_2]$ (85). Screening results showed that ligand and complexes exhibited promising biological activity with the zone of inhibition (in mm) at treatment 1000/100 (μg/μL) for compounds (80): (0.5, 0.6, 2.60); (81): (0.6, 0.5, 2.50); (82): (1.8, 2, 3.60); (83): (1, 1.1, 3.2); (84): (1.7, 1.9, 3.9) and (85): (0.9, 1, 3.4) against *E. aerogenes*, *E. coli* and *C. albicans* respectively. The zone of inhibition values of the compounds (80-85) revealed that the Zn(II) complexes (82) and (84) are potent antimicrobial agents than the Cu(II) complexes (83) and (85), followed by Cu(II) complexes than to the free Schiff bases (80) and (81).

Ngoudjou et al[54] investigated a new Schiff base tridentate heterocyclic ligand, 2-(phenyl(pyridin-2-yl) methylene)hydrazine-1-carbothioamide (86) from the condensation reaction of 2-benzoylpyridine and thiosemicarbazide and their metal complexes $[Cu(L)(NO_3)]\cdot H_2O$ (87), $[Zn(L)Cl]\cdot H_2O$ (88) and $[Ni(HL)_2](NO_3)_2$ (89) were prepared. Screening results showed that ligand and some of the metal complexes exhibited promising biological activity with the MIC (μg/mL) values (125, >125, >125, 125, 62.5, 31.25, 15.625 and 62.5); Cu(II): (31.125, 31.25, 3.9, 125, >125, >125, >125 and >125); and Zn(II): (>125, 125, 62.25, >125, 62.5, 125, 31.125 and >125); Ni(II): (>125, >125, >125, >125, >125, >125, >125 and >125) against *S. aureus*, *K. pneumoniae*, *Methicillin resistant S. aureus*, *S. flexneri*, *C. albicans* NR 29451, *C. albicans* NR 294444, *C. albicans* NR 29445 and *C. krusei* for (86), (87), (88) and (89) respectively.

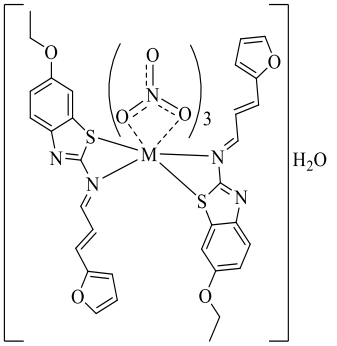
The complex Cu(II) (87) was found to be active against Methicillin resistant *S. aureus* (ATCC 33591) while the complex (88) reveals moderate activity against few pathogens. Bansod et al[8] reported a new pyrazinecarbohydrazone ligand N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene)pyrazine-2-carbohydrazide (90) and their metal complexes based on VO(IV), Cr(III), Fe(III), MoO_2(VI), WO_2(VI) and UO_2(VI) were prepared. The antibacterial studies of compounds (90-96) were carried out *in vitro* against Gram positive bacteria (*S. aureus* and *B. subtilis*) and Gram-negative bacteria (*E. coli* and *S. typhi*.) with reference to ciprofloxacin.



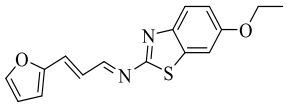
(49)



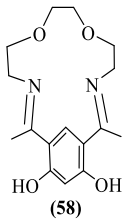
M = Fe(III), n =3 **(50)**; Co(II), n= 2, **(51)**; Zn(II), n =2, **(52)**; Zr=O(IV), n =2, **(53)**.



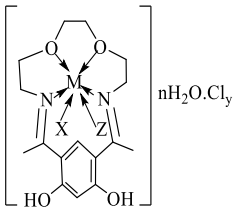
M = Gd(III) **(55)**; Sm(III) **(56)**; and Nd(III) **(57)**

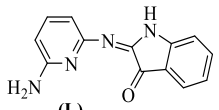


(54)



(58)

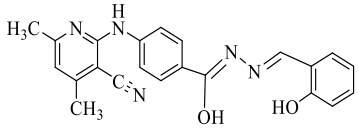




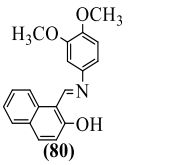
(L) **(67)**

[Cr(L)$Cl_2(H_2O)$]Cl·6H_2O **(68)**; [Mn(L)Cl]Cl·H_2O **(69)**; [Fe(L)Cl_3].6H_2O **(70)**; [Co(L)(H_2O)]Cl_2·2H_2O **(71)**; [Ni(L)Cl]Cl·H_2O **(72)**; [Cu(L)Cl$(H_2O)_2$]Cl·1.5H_2O **(73)** [Zn(L)Cl]Cl·3H_2O **(74)**; [Cd(L)$Cl_2(H_2O)$].H_2O **(75)**

M = Cr(III), X = H_2O, Z = Cl, n = 3, y = 2 **(59)**; M = Mn(II), X = Z = H_2O, n = y = 2 **(60)**
M = Fe(III), X = Z = Cl, n = 2, y = 1 **(61)**; M = Co(II), X = Z = H_2O, n = y = 2 **(62)**
M = Cu(II), X = Z = Cl, n = 4, y = 0 **(63)**; M = Ni(II), X = H_2O, Z = Cl, n = 3, y = 1 **(64)**
M = Zn(II), X = Z = Cl, n = 2, y = 0 **(65)**; M = Cd(II), X = Z = Cl, n = 1, y = 0 **(66)**

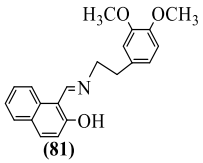


(76)



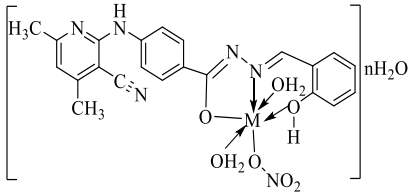
(80)

(L^1H)

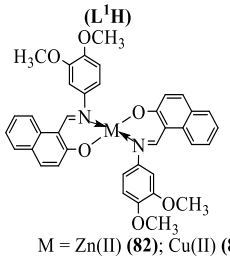


(81)

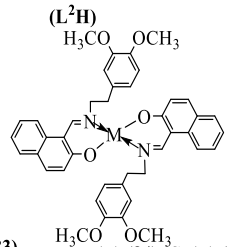
(L^2H)



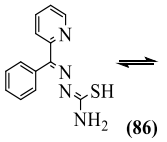
M = Co(II) **(77)**; Ni(II) **(78)**; Cu(II) **(79)**



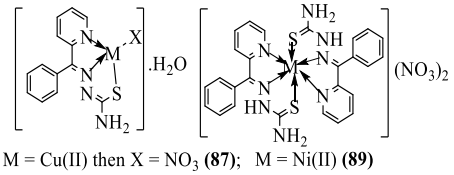
M = Zn(II) **(82)**; Cu(II) **(83)**



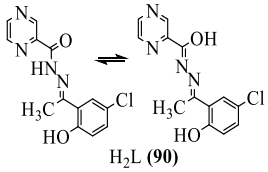
M = Zn(II) **(84)**; Cu(II) **(85)**



(86)

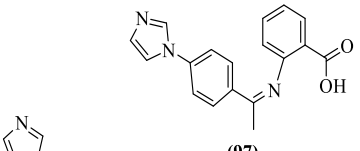


M = Cu(II) then X = NO_3 **(87)**; M = Ni(II) **(89)**
M = Zn(II) then X = Cl **(88)**

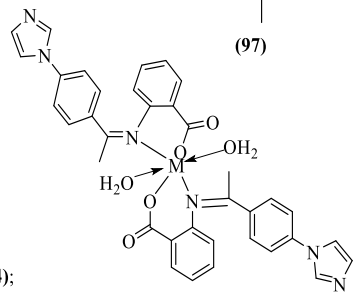


H_2L **(90)**

[VO(L)(H_2O)] **(91)**; [Cr(L)(Cl)$(H_2O)_2$] **(92)**; Fe(L)(Cl)$(H_2O)_2$] **(93)**; [MoO_2(L)(H_2O)] **(94)**; [WO_2(L)(H_2O)] **(95)**; [UO_2(L)(CH_3OH)] **(96)**



(97)



M: Cd(II) **(98)**; Co(II) **(99)**; Ni(II) **(100)**

Results showed that compounds exhibited better biological activity with the inhibition zone area (in mm) for (90): (12, 11, 11, 12, 12 and 10); (91): (20, 19, 15 and 16, 20 and 22); (92): (15, 16, 14 and 15, 18 and 17); (93): (15, 17, 15 and 14, 19 and 17); (94): (19, 20, 16 and 17, 21 and 19); (95): (16, 15, 14 and 15, 17 and 18); and (96): (15, 17, 15 and 14 , 18 and 18) against *S. aureus, B. subtilis, E. coli, S. typhi, A. niger* and *C. albicans* respectively. The significant activity for (91) seems equivalent to ciprofloxacin followed by the (94) complex. The better activity attributed due to the presence of electron withdrawing Cl group at para position (90) on aromatic ring in the molecular geometry. A comparative study of compounds exhibited that the complexes kill more aggressively than ligand against all the pathogens.

Hussein et al[33] reported a novel Schiff base 4(1H-imidazole-yl)acetophenoneanthranilic acid from condensation reaction of imidazoleacetophenone and 2-aminobenzoic acid and their metal complexes based on Co(II), Cd(II) and Ni(II) ions. *In vitro* antibacterial studies for the compounds (97-100) were performed against *S. pneumoniae, B. subtilis, P. aeruginosa* and *E. coli*, where ampicillin and gentamicin were used as standard drugs. The antibacterial screening results for Cd(II) (98) showed greatest activity with 14.6, 14.3, 11.7 and 10.8 mm inhibitory zone areas in mm, whereas Co(II) (99) and Ni(II) (100) inhibited (13.1, 10.8, 13.4 and 12) and (11.7, 13.2, 10.1 and 11.9) mm and ligand HL (97) inhibited (10.4, 11.9, NA and NA) inhibition zone areas against *S. pneumoniae, B. subtilis, P. aeruginosa* and *E. coli* respectively.

The antifungal activity of the compounds was performed against *A. flavus* and *C. albicans* by serial dilution method, where amphotericin B used as standard drug. The ligand was inactive against *A. flavus* and *C. albicans*, whereas the antifungal screening results of (98) of inhibited 16.2 and 12.5; (99) with 20 and 15.2 and (100) inhibited 10 and 12.1 mm; inhibition zone areas against *A. flavus* and *C. albicans* respectively. It revealed that metal complexes are more potent than free ligands. Rajakkani et al[60] reported the antibacterial properties of a tetradentate macrocyclic Knoevenagel Schiff base lignd (101), from condensation reaction between Knoevenagel Schiff base precursor and o-phenylenediamine and their metal complexes Cu(II) (102), Co(II) (103), Ni(II) (104) and Zn(II) (105).

The Schiff bases ligand L and its metal complexes were tested for *in vitro* antimicrobial activity against bacterial pathogens with reference to kanamycin. Results of antibacterial screening showed that MIC data (10^4 μM) for (101): (14.8, 15.4, 15.2, 16.2 and 15.8); (102): (5.6, 5.8, 5.4, 6.2 and 5.8); (103): (7.4, 7.2, 7, 7.8 and 8); (104): (7.6, 7.8, 7.4, 8.2 and 8.4); (105): (5.8, 6.2, 5.6, 6.4 and 6.2) against *S. aureus, B. subtilis, E. coli, K. pneumoniae* and *S. typhi*; respectively. Amongst all of them, Cu(II) complex (102) display significant activity and it also revealed that metal chelation increases antimicrobial activity than free ligands.

Dongare and Aswar et al[20] reported a heterocyclic N'-(4-(diethylamino)-2-hydroxybenzylidene)-4-oxopiperidine-1-carbohydrazide Schiff base ligand (106), derived by reaction of 4-oxopiperidine-1-carbohydrazide with 4-(diethylamino)-2-hydroxybenzaldehyde and their complexes- (107), (108), (109), (110), (111), (112) and (113).

The biological screening of compounds (106-113) was carried out against *E. coli, S. typhi, S. aureus, B. subtilis, C. albicans and A. niger* with reference to standard antibiotics *viz.* ofloxacin, azithromycin and fluconazole. Screening results of antimicrobial activity (inhibition zone area in mm) for (106) inhibited 8, 9, 10, 10, 11 and 9; (107) inhibited 10, 10, 11, 12, 12 and 10; (108) inhibited 11, 8, 14, 10 , 10 and 12; (109) inhibited 15, 11, 9, 9, 9 and 10; (110) inhibited 18, 15, 15, 13 , 20 and 12; (111) inhibited 16, 16, 14, 19, 15 and 15; (112) inhibited 14, 12, 12, 14, 15 and 18; (113) inhibited 19, 20, 14, 17, 25 and 13 against *E. coli, S. typhi, S. aureus, B. subtilis, C. albicans and A. niger* respectively. The maximum activity of (113) against *C. albicans* matches well with reference to fluconazole.

The significant biological activity displayed by metal complexes enables it as an important source for future studies of antimicrobial agent. Hassan et al[31] explored (OV-Azo) Schiff base ligand (114), derived by a condensation of o-vanillin and 4-aminoazobenzene and green synthesis of its metal complexes- based on Mn(II) (115), Co(II) (116), Ni(II) (117), Cu(II) (118), Zn(II) (119) and Zr(IV) (120) under microwave condition. Results of biological screening showed the inhibition zone areas in mm for metal complexes found as- (114): (NA, NA, NA, NA, NA, 13); (115): (NA, NA, NA, NA, NA, NA); (116): (19, 24, 10, 18, 25, 15); (117): (20, 20, 18,16, 16, 21); (118): (NA, 10, NA, NA, NA, NA); (119): (22, 22, 11,16, 17, 22) and Zr(IV) (120): (NA, 18, NA, NA, 8, 10), against *S. aureus, B. subtilis, S. typhimurium, E. coli, C. albicans* and *A. fumigatus* respectively.

The ligand (114) was active only against *A. fumigatus*. The metal complexes (116), (117) and (119) showed a moderate to high inhibition zone diameter and are bactericidal and fungicidal towards pathogens. The increase in activity of metal complexes was due to their effective lipophilicity. Jain et al[34] demonstrated that complexes (122-128) derived from ligand L, 2-acetyl-5-methylfuransemicarbazone (121) were potent against fungi and bacteria compared to the free ligand (L) against *C. krusei* and *C. tropicalis* and also against two different bacteria *S. aureus* and *P. aeruginosa* where chlorothalonil and neomycin were taken as a standard for testing fungal and bacterial action, respectively.

The Schiff base ligand (121) inhibited 5, 9, 18 and 11 mm and their metal complexes displayed higher activity, (122) inhibited as 14, 9, 27 and 34 mm; (123) as 23, 9, 27 and 23 mm; (124) as 27, 10, 36 and 43 mm; (125) as 25, 14, 38 and 43 mm; (126) as 9, 11, 23 and 27 mm; (127) as 16, 11, 23 and 27 mm; (128) as 25, 20, 38 and 43) mm; (129) as 34, 25,

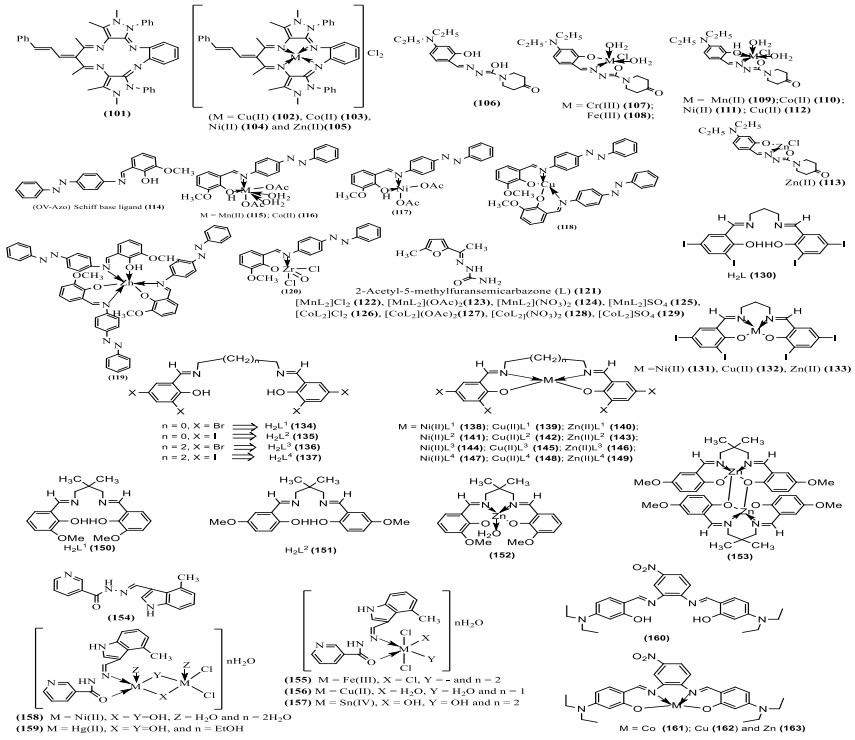
34 and 34 mm inhibition zone areas towards *S. aureus* and *P. aeruginosa*, *C. Krusei* and *C. tropicalis* at 1000 ppm concentration respectively. The above results revealed that metal complexes cause significant inhibitory effect against pathogens and could turn into an effective antimicrobial agent in future medicinal field.

Kargar et al[37] synthesized a new series of complexes obtained by 1, 3-diaminopropane and 3, 5-diiodosalicylaldehyde and their Zn(II), Cu(II) and Ni(II) complexes. Screening results showed that ligand and some of the metal complexes exhibited marvelous biological activity with inhibition zone area (in mm) values 13, 13, 15, 14 against *E. coli*; 12, 15, 14, 15 against *P. Aeruginosa*; 25, 27, 27, 28 against *S. aureus*; 21, 23, 22, 24 against *Bacillus cereus*; for (130), (131), (132) and (133) respectively where erythromycin and Ampicillin used as reference. It was found that all the compounds (130-133) are potent against bacterial strains in comparison with the standard drugs and therefore, they may be suitable candidate to discover alternative drugs.

Kargar et al[38] synthesized a series of four salen-type Schiff base ligands H_2L^1 (134), H_2L^2 (135), H_2L^3 (136) and H_2L^4 (137) by condensation reaction between 3,5-dihalo-salicylaldehyde and their respective diamine and their respective nickel(II), copper(II) and zinc(II) complexes (138-149). Screening results showed that compounds exhibited significant biological activity with the inhibition zone area (in mm) values 12, 12, 22, 19 for H_2L^1 (134); 12, 12, 26, 22 for H_2L^2 (135); 15, 13, 21, 23 for H_2L^3 (136); 11, 12, 25, 22 for H_2L^4 (137); 14, 13, 24, 22 for NiL^1 (138); 13, 14, 23, 21 for CuL^1 (139); 14, 14, 24, 23 for ZnL^1 (140); 14, 13, 27, 24 for NiL^2 (141); 14, 13, 27, 25 for CuL^2 (142); 13, 15, 29, 26 for ZnL^2 (143); 17, 15, 22, 25 for NiL^3 (144); 16, 14, 23, 26 for CuL^3 (145); 16, 15, 24, 25 for ZnL^3 (146); 13, 13, 26, 24 for NiL^4 (147); 13, 13, 27, 24 for CuL^4 (148); 12, 13, 27, 25 for ZnL^4 (149) towards *E. coli*, *P. Aeruginosa*, *S. aureus* and *B. cereus* respectively.

The inhibition zone area produced by the tested compounds revealed that it is more potent inhibitor of Gram-positive bacteria (*S. aureus*, *B. cereus*) rather than Gram-negative bacterial strains (*E. coli*, *P. Aeruginosa*) as comparable to erythromycin and ampicillin standard drugs. Two new Schiff base H_2L^1 (150) = [6,6′-((1E,1′E)-((2,2-dimethylpropane-1,3-diyl)bis(azanylylidene))bis(methanylylidene))bis(2-methoxyphen- ol)] and H_2L^2 (151) = [2,2′-((1E,1′E)-((2,2-dimethylpropane-1,3-diyl)bis(azanylylidene))bis(methanylylidene))bis(4-methoxyphenol)]) and their zinc(II) Schiff base complexes (152 and 153)[39] were synthesized.

Results of antibacterial and antifungal screenings were performed with reference to chloramphenicol and Clotrimazole, which showed that the inhibition zone areas in mm for ligands and their zinc(II) complexes as- H_2L^1 (150): (12, 12, 9, 10, NA); H_2L^2 (151): (10, 10, 11, 9, 12); (152): (16, 15, 11, 12, 22) ; (153): (18, 14, 13, 12, 23) against *S. aureus*, *B. cereus*, *E. coli*, *P. Aeruginosa*, *C. albicans*, respectively. The antifungal screening of ligands and zinc complexes in percentage mean mycelial inhibition were found for H_2L^1 (150): 21.4 %; H_2L^2 (151): 21.4 %; (152): 22.8 %; (153): 22.8 against *A. brasiliensis*. On inspection, the antimicrobial activities of both (152) and (153) were higher than that of their respective ligands. The complexes showed potent antifungal activity against *C. albicans*, contrary to this no such activity was observed against *A. brasiliensis*.



El-Gammal et al[24] reported synthesis of (E)-N'-((4-methyl-1H-indol-3-yl)methylene) nicotinohydrazide (154) from condensation of nicotinohydrazide and 4-methyl-1H-indol-3-carbaldyhde and its novel mononuclear Fe(III) (155), Cu(II) (156), Sn(IV) (157), binuclear Ni(II) (158) and Hg(II) (159) complexes. Further the complexes were screened against Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*). Antibacterial screening results for dinuclear $[Hg_2(HL)Cl_4]$.EtOH complex (159) towards *S. aureus* and *E. coli* inhibited 34, 30 mm mg^{-1} respectively, even better than standard ampicillin drug. Results revealed that the ligand is active against both the bacterial strains *S. aureus* (11 mm mg^{-1}) and *E. coli* (11 mm mg^{-1}).

All the complexes exhibited significant antibacterial activity against *S. aureus* and *E. coli* than free ligand. The antibacterial activity of the compounds is shown in order:

Hg(II) > ampicillin > Sn(IV) > Cu(II) > Ni(II) > HL for *S. aureus*
Hg(II) > ampicillin > Cu(II) > Sn(IV) = Ni(II) > HL for *E. coli*

The antifungal activity of compounds was investigated against *A. flavus* and *C. albicans*. Screening results showed that (157) and (158) were inactive against *Aspergillus flavus*, complex (156) exhibited moderate activity while the binuclear $[Hg_2(HL)Cl_4]$.EtOH (159) showed excellent activity against fungal strain *A. flavus*, even better than Amphotericin B. The ligands (154), Sn(IV) (157) and Ni(II)(158) were inactive against *C. albicans* but Cu(II)(156) exhibited moderate activity towards *A. Flavus* and with *C. albicans*, all compounds exhibited moderate activity. It showed that the lower polarity in chelated metal complexes leads to an increase in zone inhibition rather than free ligand. Venkatesh et al[76] synthesized a salen-type Schiff base ligands H_2L (160) by condensation of 4-nitrobenzene-1,2-diamine with 3−4- (diethylamino)-2-hydroxybenzaldehyde and their respective Co(II), Cu(II) and zinc(II) complexes (161-163).

Screening results showed that compounds exhibited significant *in vitro* antibacterial and fungal activity and aggressively kills microorganisms compared to free ligand (160). Results showed that (161) and (162) complexes are effective towards *A. niger, E. Coli, K. pneumoniae*; (162) and (163) are active against *P. vulgaris*, in addition, the (163) complex exhibited significant activity towards *R. bataticola*. Arulmozhi et al[7] investigated novel 2-((E)-(((E)-(1H-pyrrol-2-yl)methylene) hydrazineyl idene)-methyl)phenol [HL] (164) by reaction of 5-(diethylamino)-2-hydroxybenzaldehyde and (E)-2-(hydrazineylidenemethyl)- 1H-pyrrole and their metal complexes (165-172).

Results of the antibacterial study of all metal complexes was well-documented in the table 1 towards *E. faecalis, S. aureus, K. pneumonia and A. baumannii*. In this series, Cu(II) complex (171) displayed highest activity, the reason for this may be due to presence of planar 4,4'-bipyridine moieties, which is a strong intercalator and fits into the grooves of the double-helix DNA strand causing significant damage. In addition, increase in the lipophilic character of the chelated compound facilitates their permeation through the lipid layer of the bacterial cell membrane lead to an increase in inhibition zone area rather than free ligand.

Latif et al[44] synthesized benzyl N'-(4-dimethylaminobenzylidene) hydrazinecarbodithioate (173) derived from 4-(dimethylamino)benzaldehyde and S-benzyldithiocarbazate and its metal complexes Ni(II), Cu(II) and Zn(II) (174-176) and and also investigated their antibacterial activity against Gram- negative bacteria (*E. coli* and *S. sonnei*) and Gram-positive bacteria (*B. subtilis*) by using diffusion method where kanamycin was used as standard drug. Results of antibacterial activity testing results showed that the inhibition zone area (in mm) values 13, 14 and 13 for (173); 16, 15 and 17 for (174); 18, 16 and 19 for (175); 14, 13 and 15 for (175) towards *Escherichia coli, S. Sonnei* and *Bacillus subtilis* respectively. The complexes were more potent antibiotics than the free ligand. The (174) and (175) complexes displayed high antibacterial activity whereas, (176) was moderately active.

Keypour et al[41] have reported Schiff base ligand, 1,4-bis(o-aminobenzyl)-1,4-diazacycloheptane (177) and their Ni(II) (178) and Cu(II) (179) complexes.

Table 1
Antibacterial activity of Metal complexes (165-172) against bacterial strains

	Inhibition zone area in mm			
Complexes	***E. faecalis***	***S. aureus***	***K. pneumoniae***	***A. baumannii***
165	5.1 ± 0.5	5.6 ± 0.5	4.3 ± 0.5	3.8 ± 0.5
166	6.8 ± 0.5	6.3 ± 0.	NA	NA
167	5.9 ± 0.5	5.5 ± 0.5	6.3 ± 0.5	6.4 ± 0.5
168	5.9 ± 0.5	6.2 ± 0.5	6.8 ± 0.5	5.6 ± 0.5
169	6.4 ± 0.5	5.8 ± 0.5	8.2 ± 0.5	4.3 ± 0.5
170	9.2 ± 0.5	8.4 ± 0.5	NA	NA
171	10.8 ± 0.5	10.5 ± 0.5	13.3 ± 0.5	11.1 ± 0.5
172	9.4 ± 0.5	8.7 ± 0.5	13.2 ± 0.5	10.2 ± 0.5
Ciprofloxacin	17.8 ± 0.5	15.5 ± 0.5	18.4 ± 0.5	14.5 ± 0.5

They tested antibacterial activity against bacterial species *E. coli* and *S. aureus*. Antibacterial screening results against *E. coli* and *S. aureus* were compared with chloramphenicol drugs and it was reported that the (177) inhibited 7.3 and 8 mm, whereas metal complexes- (178) inhibited 10.3 and 12mm and (179) inhibited 15.5 and16 mm inhibition zone areas against *E. coli* and *S. aureus* respectively. It showed that metal complexes are more effective against all the bacterial strains as compared with the parent Schiff base ligand.

Anacona et al[6] synthesized a novel Schiff base obtained from phenoxymethylpenicillin and 1,2-diaminobenzene and their metal complexes having the general formula $[ML(OAc)(H_2O)_2]$ where M = Fe(II) (181), Co(II) (182), Ni(II) (183), Cu(II) (184) and Zn(II) (185).

The antibacterial activity was screened with the help of agar disc diffusion method and the minimal inhibitory concentration (MIC) by serial tube dilution technique against Gram-positive bacterial strains. The screening results were compared with the activity of the standard drug phenoxymethylpenicillin. Results showed that (180) inhibited (15, 24, 16, 17 and NA) mm; (181) inhibited (20, 30, 25, 22 and 15) mm; (182) inhibited (NA, NA, 16 and NA) mm; (183) inhibited (10, 40, 36, 27 and 18) mm; (184) inhibited (NA, 36, 7, NA and 15) mm; (185) inhibited (NA, NA, 7, NA and NA) mm inhibition zone areas against *S. viridans, Enterococcus sp, S. aureus, E. faecalis* and *Methicillin-resistant S. aureus* respectively. It was also observed metal complexes of (181), (183-184) exhibited much better bactericidal activity.

Ommenya et al[55] investigated Schiff bases ligand 4-chloro-2-{(E)-[(4-fluorophenyl)imino]methyl}phenol synthesized from the condensation reaction of 5-chlorosalicylaldehyde and 4-fluoroaniline. The antibacterial activity was screened *in vitro* against Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and Gram-positive bacteria (*Bacillus subtilis and Staphylococcus typhi*) by using disc diffusion method and amoxyclav (AMC), nalidixic acid (NA) and gentamicin (GEN) act as the standard drug against all the bacterial strains.

Antibacterial study of the compounds is shown as follows: HL ligand (186) showed inhibition zone area 7.3, 8.4, 7.7 and 8.4 mm; Mn(II) (187): 8.1, 10.7, 9.7 and 9.3 mm; Co(II) (188): 9, 9.7, 8.3 and 9.4 mm; Ni(II) (189): 9.5, 11.3, 9.7 and 8.6 mm; Cu(II) (190): 8.1, 10.3, 8.6 and 8.7 mm; Zn(II) (191): 7.6, 10, 8.4 and 10.1 mm at 10 μg/ml concentration against *E. coli*, *P. aeruginosa*, *B. subtilis* and *S. typhi* respectively. The metal complexes show greater antibacterial activity as compared to free Schiff base ligand.

Mahmood et al[49] studied heterocyclic Schiff base (E)-2-((4-(1H-benzo[d]imidazol-2-yl)phenylimino)methyl)-4-bromo phenol (192) and their Zn(II) (193), Ni(II) (194), Cu(II) (195) and Pd(II) (196) complexes. The antibacterial activity was screened against *M.luteus*, *E. coli* and *E. aerogenes* measured with the help of disc diffusion method. Results of antibacterial activity for (192) displayed inhibition zone area in mm as 6, 17 and 9; Zn(II) (193): 11, 18.9 and 13.6; Ni(II) (194): 16.8, 18.8 and 13; Cu(II) (195): 14.9, 11.8 and NA; Pd(II) (196): 9, NA and 12; against *Micrococcus luteus*, *Escherichia coli* and *Enterobacter aerogenes* respectively. Results showed that that metal complexes were more active against bacteria than the ligand except (195) and (196), which were inactive against *E. coli* and *E. aerogenes*, respectively.

Hashem et al[30] synthesized Schiff base ligand, N'-(4-hydroxy-3 methoxybenzylidene) nicotinohydrazide (L_1) (197) and N'-((2-chloroquinolin-3-yl)methylene)nicotine hydrazide (L_2) (198) and its metal complexes L_1-Co(II) (199), L_1-Cu(II) (200), L_2-Co(II) (201) and L_2-Cu(II) (202),.

The synthesized compounds were checked for their anti-bacterial activity against *S. aureus, B. subtilis, E. coli* and *P. vulgaris* through disc diffusion method, where gentamycin used as standard.

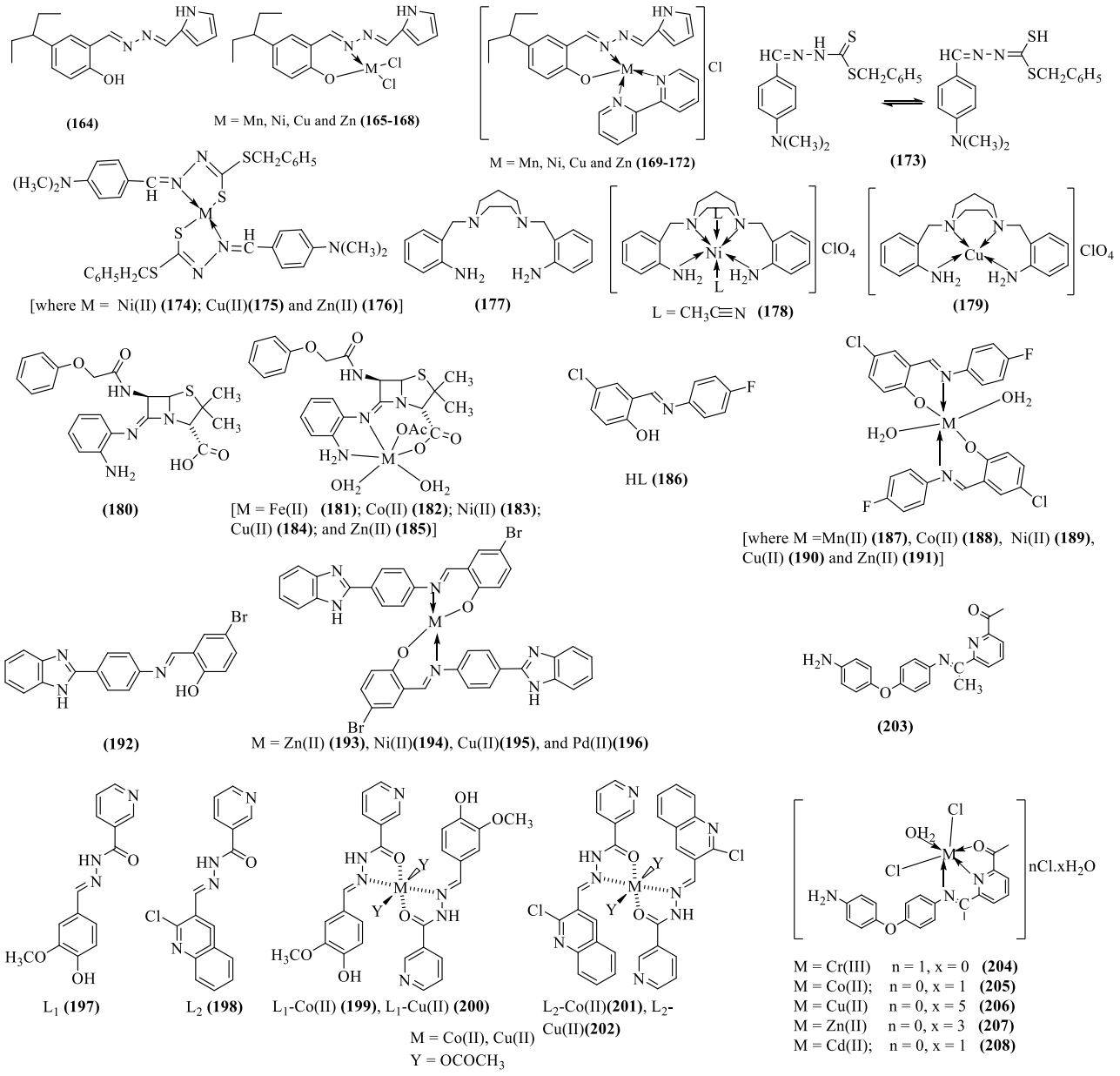
Screening results of antibacterial activity (inhibition zone area in mm) for (197) inhibited 10, 9, 11 and 15; (198) inhibited 5, 8, 10 and 13; (199) inhibited 13, 12, 15 and 19; (200) inhibited 12, 11, 12 and 13; (201) inhibited 9, 12, 14 and 18; (202) inhibited 6, 10, 13 and 16 against *S. aureus, B. cereus, E. coli, P. vulgaris* respectively.

It showed that the metal complexes illustrate the moderate antibacterial activity against *S. aureus, B. subtilis, E. coli*, but maximum activity against *P. vulgaris*. Finally, it was visualized that the metal complexes (199-202) showed higher antibacterial activity than the free ligands (L_1 and L_2).

Deghadi et al[17] also have reported Schiff base 1-(6-(1-((4-(4-aminophenoxy)phenyl)imino)ethyl)-pyridin-2-yl)ethan-1-one (203) and their transition metal complexes (204-208). The Schiff base ligand was prepared by condensation of 4,4-oxydianiline with 2,6-diacetyl-pyridine. All the compounds were screened for their *in vitro* activity toward a number of bacteria.

Screening results showed that compounds exhibited significant biological activity with the inhibition zone area (in mm) values 9, NA, NA, 9 for (203); 9, 11, 9, 13 for Cr(III) (204); 21, 15, 15, 15 for Co(II) (205); 21, 15, 15, 15 mm for Cu(II) (206); 14, 16, 13, 14 mm for Zn(II) (207); 12, 15, 11, 12 mm for Cd(II) (208) towards *B. subtilis, S. aureus, E. coli and P. aeruginosa*, respectively.

The Schiff base ligand (203) was found to be biologically active against *B. subtilis* and *P. aeruginosa* while it was inactive against *E. Coli* and *S. aureus*. Some of these metal complexes like Cr(III), Co(II), Zn(II) and Cu(II) act as effective drugs than the free ligand and are well illustrated by literature survey.



Conclusion

Schiff base metal complexes give enthusiasm among professionals and researchers to design and develop methodology for the treatment of various diseases. Nevertheless, it is necessary to control resistance of antimicrobial effect using a multiple strategy awareness program displaying the adverse effect of antimicrobial resistance, using antimicrobials drugs when required. This review deals with the application of novel Schiff bases metal complexes having tremendous potential against pathogens.

It was found that d and f block metal complexes have been used as potent drugs. Pharmacologists need to pay more attention. So far, most of current studies on metal Schiff-base complexes only focused on screening *in vitro* activity. In addition, *in vivo* and clinical trials are required. Schiff-base metal complexes may be promising antimicrobial agents in clinical trials.

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