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Antibacterial and Antifungal Activity of Schiff Bases and their Metal Complexes

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ABSTRACT

Schiff bases are typically synthesized by the condensation of amines and a carbonyl bearing compounds. Schiff bases are important intermediates for the synthesis of various bioactive compounds. These compounds and their metal complexes are very important as catalysts in various biological systems, polymers, and dyes, medicinal and pharmaceutical fields. Furthermore, they are reported to show a variety of biological activities including antibacterial and antifungal activities.

Introduction

Schiff bases are organic compounds derived from an amine and carbonyl compounds[1-8]. They are important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively [9-16]. In azomethine chemistry, the C=N linkage is essential for biological activity[17], several azomethines were reported to possess remarkable biological activities, anticancer and herbicidal activities [18]. Schiff bases also have wide applications in food industry, dye industry, catalysis, antiviral activity, antiinflammatory, corrosion inhibitor, and agrochemical applications [19,20].

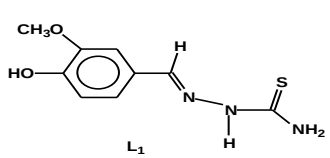
They also play vital roles in pharmaceuticals and rubber additives[21], and as amino protective group in the synthetic organic chemistry and several biologically active compounds[22-24], they are also used in analytical [25], medicinal [26,27] and polymer chemistry [28,29]. There has been increasing demands on the screening of new and more effective antimicrobial drugs with low toxicity. Schiff-base are considered to be of the most important organic compounds with the potential to form coordination compounds with main group and transition metal due to their preparative accessibility and structural variety[30].

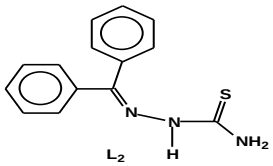
ligands containing donor atoms like N, O, S show broad biological activity and are of special interest because of the variety of ways in which they are bonded to metal ions. [31]. It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities. [32,33]

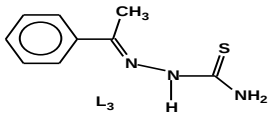
The rapid development of these ligands resulted in an enhance research activity in the field of coordination chemistry leading to very interesting conclusions. This review concentrates on the synthesis , antibacterial and antifungal activity of schiff bases and their transition metal complexes.

Antibacterial and Antifungal Activities

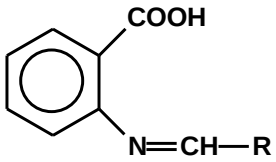
Schiff bases derived from thiosemicarbazide and ketones(vanillin L_1, benzophenone L_2, and acetophenone L_3) [34] were used to study their antibacterial activities against some pathogenic bacteria. The benzophenone (L_2) schiff base show significant antibacterial activity as compared to that of Kanamycin(control).







Schiff basis of anthranilic acid have been screened for their in vitro growth inhibitoin activity against different strains of bacteria and fungi, their activities are comparable to that of standards such as Gentamycin and Fluconazole. Compound 1b exhibit the highest antibacterial activity while compound 1a shows the best anti fungal activity[35].



1a-1d

R= o-hydroxyphenyl (1a), p-hydroyphenyl (1b), furfuryl(1c), p-nitrophenyl (1d)

Titaniun complexes of composition $[TiCl_2(SB)_2]$ where SBs (A1= tetracycline schiff base, B1=streptomycin, C1= ceffixine, D1= ampicillin schiff base), the synthesized complexes were tested for their antimicrobial activities against*B- cereus, M. luteus, S.aureus, S. epidemidis, A. hydrophila, A. faecalis, S. sonnei, K. peneumoniae, P. aeruginosa* and *S. typhimurium.* It was found that the metal complexes are more active than their parent schiff bases[36].

A new series of transition metal complexes [37]of Cu(II), Ni(II) Co(II), Mn(II), Zn(II), VO(II), Hg(II), Cd(II) have been synthesized from the schiff base L derived from 4-

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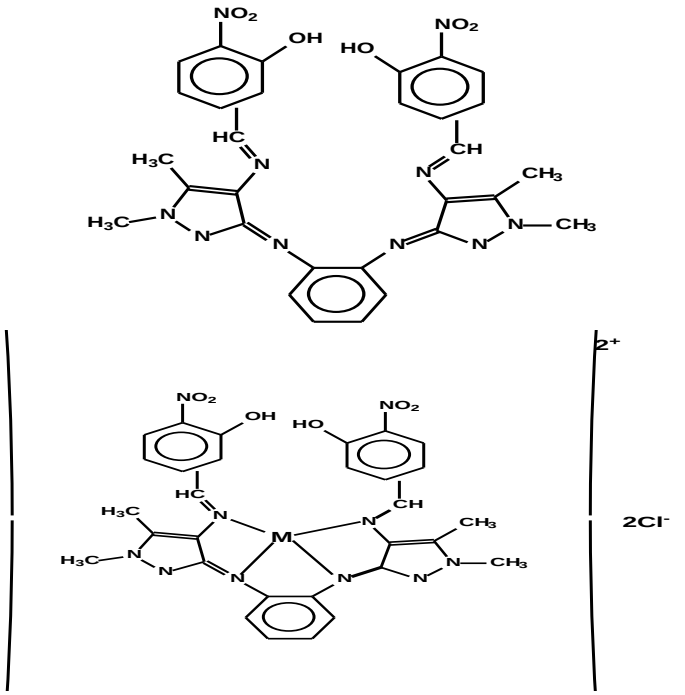
aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and o-phenylenediamine. Antimicrobial screening tests gave good results in the presence of metal ions coordinated to the ligand.



Schiff bases derived from 3-substituted-4-amino-5-mercapto-1,2,4-triazole and glyoxal/ biacetyl/benzyl together with their oxovanadium (IV) and dioxouranium(VI) were synthesized and characterized, some of these complexes were screened for their antibacterial activities against *E. Coli* and *B. Cirrafigellosus*, and antifungal activities against *C.Albicans* and *A. nigar*. The data indicate that most of oxovanadium (IV) complexes are more active than the free ligands and the dioxouranium(VI) complexes[38].

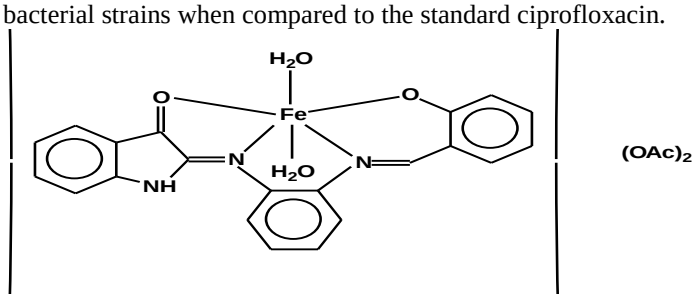
Osowole et al [39] reported on the synthesis and antibacterial activities of schiff bases containing aminoindane moiety and their complexes with VO(II), Mn(II), Co(II) and Ni(II). The in vitro antibacterial activities of these complexes and the free ligands against different bacterial strains shows that, HL_1 and its complexes are more active than HL_2 and its metal complexes, and the later have selective inactivity against *Bacillus cereus* and *klebsiella oxytoca.*

Schiff bases and their metal complexes[40], were tested agaist *Staphylococcus aureus, Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa and Klebsiella oxytoca*. The Pd(II) complex is the only one that is active against *S. aureus*, the resistance of *P. aeruginosa* to all compounds is due to a concerted action of multi drug efflux pumps and the law permeability of the bacterial cellular envelopes[41]. While the resistance of *Staphylococcus aureus* has been attributed to the production of β- lactamase which inactivates the compounds[42].

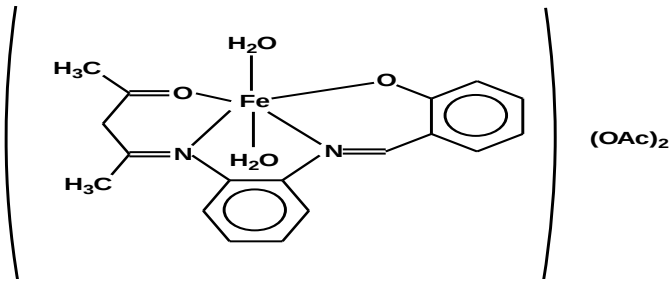
Schiff bases of 5-acetamido-1,3,4-thiadiazole-2-sulphonamide complexes of the general formula ML2, where M= Mn(II), Fe(II), Ni(II), Cu(II) were screened for their fungicidal activity against *A. niger* and *A. flavus*. From the results it can be observed that the complexes show greater activity than the free ligand[43].

Schiff base derived from N-aminopyrimidine-2- thione and 5-bromosalicylaldehyde and its complexes of Cu(II), Ni(II), Co(II), Pd(II), Pt(II) were screened for their antimicrobial activities. The schiff base and its Cu(II), Co(II) complexes show good biological activities against all tested bacteria and yeast strains[44].

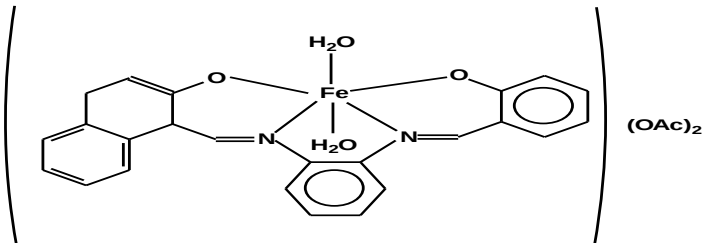
The synthesis and antibacterial activity of schiff bases obtained by the condensation of o-phenylenediamine, salicylaldehyde and isatin/ 2-hydroxy Naphthaldehyde/ acetylacetone and their Fe (III) complexes were screened for their antibacterial activities [45], against *Staphylococcus aureus* (gram positive) and *Escherichia* coli (gram negative) the complexes were found to be of better activity against both bacterial strains when compared to the standard ciprofloxacin.



FeL1



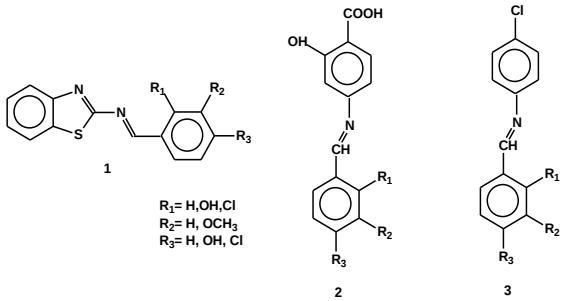
FeL2



FeL3

Schiff bases obtained from methylthiosemicarbazone and 5-formyl-6-hydroxycoumarin/8-formyl-7-hydroxy-4-methylcoumarin and their Co(II), Ni(II), and Cu(II) were investigated for their antibacterial activities[46]. All complexes show potential antibacterial activity against all bacterial strains than the activities of the free ligands.

Three new schiff bases were screened for their biological activity against bacteria, fungi and yeast, together with their metal complexes. The complexes show more potent activities compared to the schiff base ligands [47].



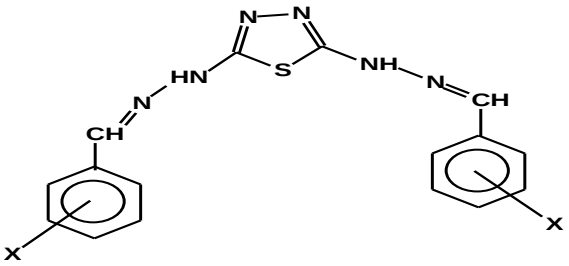
various new quinolin-2-(1H)-one- triazole derived schiff base ligands and their Cu(II) and Zn(II) complexes were investigated for their anti bacterial activities, the Zn(II)

complexes showed an increased activities compared to the corresponding free ligands [48].

Schiff base derived from indoline-2, 3-dione and 2-aminobenzoic acid and its Tin complex showed antibacterial activity against *Staphylococcus aureus*. The results compared with standard drug (Imipinem) have indicated that compounds were active but activity was lesser than the standard drug. This activity might be due to the presence of a hydroxyl and phenyl group [49].

The increased activity of the organotin complexes may be due to the coordination and polarity of tin (IV) atom with ligand oxygen. The order of increasing activities is ligand < MeSnL < PhSnL < BZ3SnL, the results matched with the previously reported data for the biological activity of organotin complexes [49].

The synthesis and biological activities of some schiff bases of imidazo-[2,1b]-1,3,4-thiadiazole derivatives were reported.[50]. The synthesized schiff bsaes were subjected to antimicrobial screening, they show moderate to good activities when compared to the standard antibiotic ampicillin.

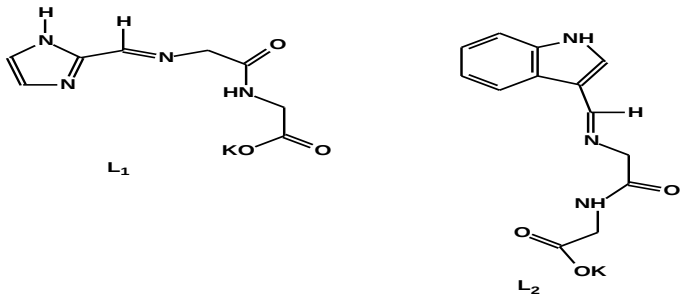


3-5

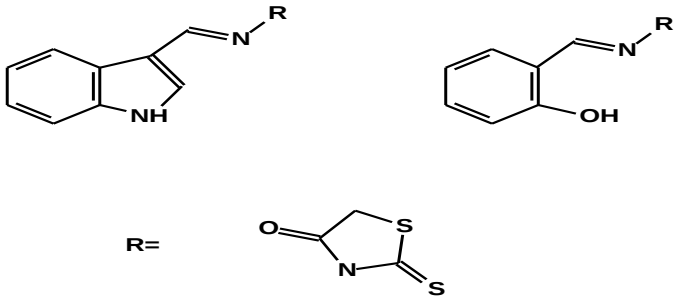
3, X= m-NO2, 4, p-NO2, 5, p-OH

Mixed ligand transition metal complexes of Cu+2, Ni+2 and Co+2 ions with Schiff base ligands derived from the condensation of o-hydroxy benzaldehyde with amino phenols and nitrogen donor amine bases was reported.The authors have also studied the antibacterial and antifungal activities of the compounds[51].

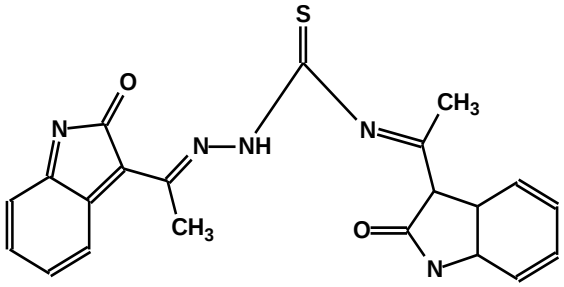
The in vitro biological screening of L1, L2, and their Zn (II) complexes were studied against some bacterial and fungal species. The inhibition values of the schiff bases and their complexes indicate that the complexes exhibit higher antimicrobial activities than the free ligands [52].



Some transition metal complexes with Schiff bases derived from 2-formylindole, salicylaldehyde and N-amino Rhodanine. The free ligands and their metal complexes were also screened for antimicrobial activities against *Bacillus cerens, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and *Candida albicans*. The results indicated that the ligands do not have any activity, where as their complexes showed more activity against the same organisms under identical experimental conditions [53].



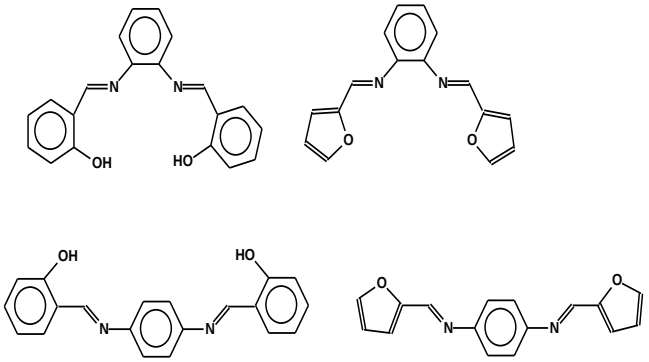
Antimicrobial potency was seen among schiff base ligand (L) and its Ni (II), Cu(II) and Co(II) complexes. The activity of complexes is higher than the free ligands. The Ni (II) complex shows the highest antimicrobial activity [54].



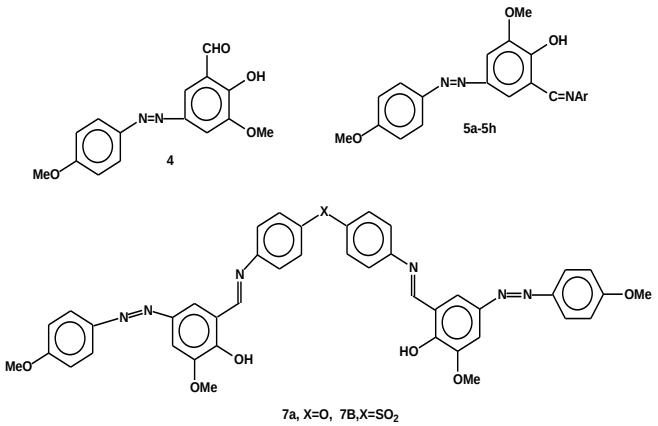
L

Mixed ligand complexes of o-vanillidene-2-aminobenzothiazole and 1,10- phenanthroline has been screened for their in vitro biological activities against *Escherichia coli, Pseudomonas aeruginosa, Salmonella Typhi* and *Vibrio parahaemolyticus* by well diffusion method using agar nutrient[55].

Platinum complexes of schiff base ligand derived from salicylaldehyde and 2-furaldehyde with o-phenylenediamine and p-phenylenediamine show more activity against various bacterial and fungal strains than the free ligands [56].



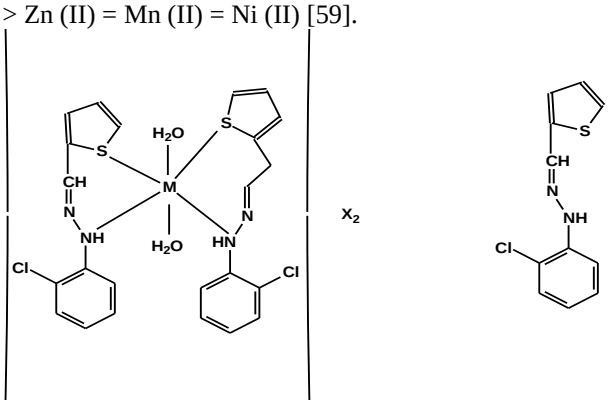
New azo schiff bases derived via condensation of different aromatic amines and a new azoaldehyde, 2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde. All the new compounds were tested against five microorganisms. *S. aureus, B. subtilis, K. pneumonia, P. aeruginosa* and *E. coli*. Compounds 4, 5a, 5c, 5d, and 5g were moderately active against *S. aureus, B. subtilis*. Compound 7b was highly active against *B. subtilis* and moderately active towards *S. aureus*. The other compounds were inactive against the investigated bacterial species. The antifungal activities of the synthesized schiff bases were tested against eight different fungal species. None of these compounds show activity towards fungi species under investigation [57].



7a, X=O, 7B,X=SO_2

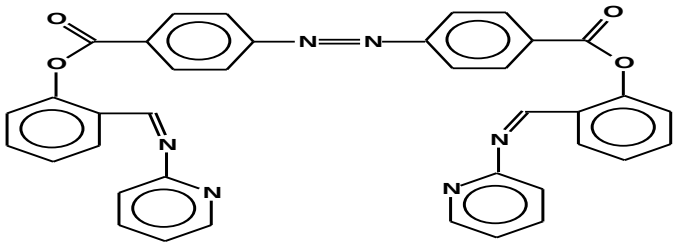
Complexes of Co(II),Cu(II),Ni(II),Mn(II) and Cr(III) with Schiff bases derived from 2,6-diacetylpyridine and 2-pyridine carboxaldehyde with 4-amino-2,3-dimethyl-1-phenyl- 3-pyrozolin-5-one show antibacterial and antifungal activities against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Mycobacterium Smegmatis, Pseudomonas aeruginosa, Enterococcus cloacae, Bacillus megaterium* and *Micrococcus leteus*. The results showed that L_1 ligand has a greater effect against *E. coli* than the other bacteria while it has no activity against *S. aureus*. Metal complexes have a greater effect than L2 against almost all bacteria [58].

Metal chelates of the general formula [M(HL)2(H"O)2]X2, where M= Mn(II), Co(II), Cu(II), Ni(II), Zn(II), X= NO3 or Cl have been screened for their in vitro antibacterial activity against (*E. coli* and *S. aureus*, and two fungus *Aspergillus flavus* and *Candida albicans*. The metal complexes show more anti bacterial activity than the free ligands. The antifugal activities of the above mentioned complexes follow the order Cu (II) >Co (II) > Zn (II) = Mn (II) = Ni (II) [59].



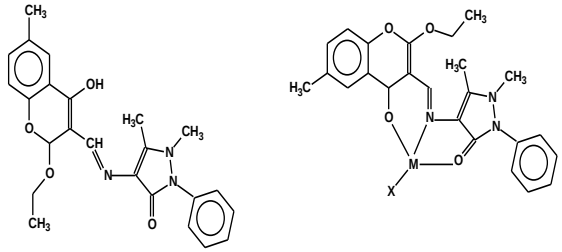
The Schiff base 4-chloro-2-(2-morphiolinoethylimino) methylphenolato methanolchloro and its Zn(II) complex were screened for antibacterial activity against two Gram positive bacterial strains (*B. subtilis* and *S. aureus*) and two Gram-negative bacterial strains(*E. coli* and *P. fluorescence*) by the MTTmethod. The Schiff base showed significant activity against two Gram-negative bacterial strains with MIC of 12.5µgmL-1but was inactive against two Gram negative bacterial strains. The Zn complex showed a wide range of bactericidal activities against the Gram positive and Gram negative bacteria, were potent than, or similar with commercial antibiotics (Kanamycin and penicillin) [60].

A new heterocyclic schiff base ligand (L) bis-(pyridin-2-yl imino) phenyl)-4,4`-(diazene-1,2-diyl)-dibenzoate(BPPD,L) and its complexes with divalent metal ions Co(II), Cu(II), Ni(II), Zn(II) have been screened for their antibacterial activity towards *S. aureus* and *E.coli*. Their antifungal activities against *A. niger* and *C. albicans* were also investigated. The results show that complexes have higher antibacterial activities than the ligands in the order Cu(II)L > Zn(II))L > Ni(II)L > Co(II)L > L [61].



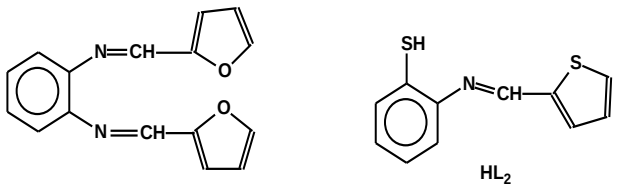
(BPPD,L)

Schiff base obtained through the condensation of 4-amino-2, 3-dimethyl-1- phenyl-3-pyrazolin-5-one with 3-formyl-6-methyl-chromone and its complexes with Cu(II), Ni(II), VO(II), Mn(II) were evaluated for antibacterial activity. The activities show that the schiff base became more active upon formation of complex [62].



Bidentate complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with benzofuran-2-carbohydrazide and benzaldehyde [BPMC] or 3,4-dimethoxybenzaldehyde[BDMePMC] showed biological activities. Co (II) and Cd (II) complexes of [BPMC] are moderately active toward *E.coli* whereas Cu(II), Zn(II) and Ni(II) complexes of [BPMC] and Cu(II) and Zn(II) complexes of [BDMeOPMC] are more active against *S.aurious* as compared to free ligands. None of the complexes are active against A.niger, but in the case of *A.fumigatus*, Cu(II),Co(II), Ni(II) and Cd(II) complexes of [BDMeOPMC] are more active than the parent ligands[63].

Metal complexes of schiff bases derived from 2-furancarboxaldehyde and o-phenylenediamine (L_1) and 2-thiophenecarboxaldehyde and 2-aminothiophenol (HL_2), were screened for their antibacterial and antifungal activities. The activity data show that the metal complexes are more potent antibacterial agent than the parent schiff base ligands [64]. All metal complexes of L_1 and Fe(III), Zn(II), and UO2(II) complex of HL_2 inhibit fungal growth at high concentrations more than the parent ligands and standards.



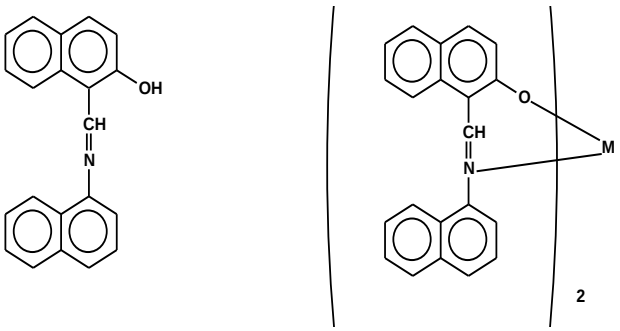
L_1 HL_2

Schiff bases containing 2,4-dichloro-5-fluorophenyl moieties also take part in effective inhibition of bacterial growth [65].

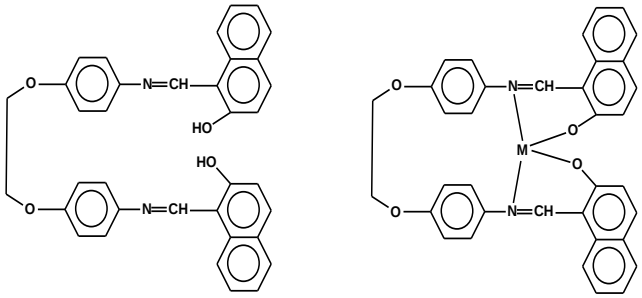
Ni(II) and Cu(II) complexes of HL and H_2L were synthesized and screened for their antifungal activity, the complexes were more active than the free ligands[66].

On the other hand, the compounds obtained from furylglyoxal and p-toluidene show antibacterial activity against: *Escherichia coli, Staphylococcus aureus, Bacillus subtilis* and *Proteus vulgaris*. Isatin derived Schiff bases present anti-HIV and antibacterial activity. Other Schiff bases derivatives, which

possess antibacterial activity are: benzimidazole, thiazole, pyridine, glucosamine, pyrazolone, hydrazide, thiazolidiones, indole, thiosemicarbazone, p-fluorobenzaldehyde [67].

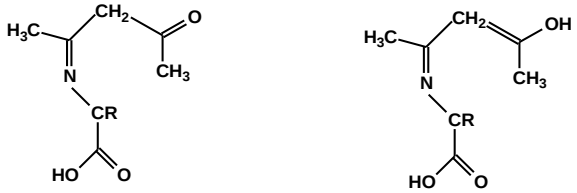


HL M(HL)2 (M= Cu, Ni)

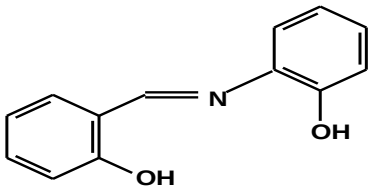


H2L MH_2L (M= Cu, Ni, Zn), $CoH_2L.2H_2O$

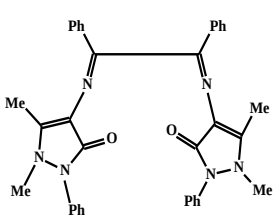
Amino acid Schiff base derived from 2- hydroxy-5-methylacetophenone and glycine and its transition metal complexes showed bacterial activities. The ligand was bacteriostatic against all bacterial strains except *Proteus vulgaris*, *Shigella flexneri*, and *Bacillus coagulans*. All complexes are either resistant or less sensitive against P.vulgaris. However compared to the antibacterial activity of the standard antibiotic streptomycin, the activity exhibited by the ligand and metal complexes was lower. The metal complexes showed to exhibited higher activity than the free ligand against the same organism under identical experimental conditions, such increased activity of the metal chelates can be explained on the basis of chelation theory [68].



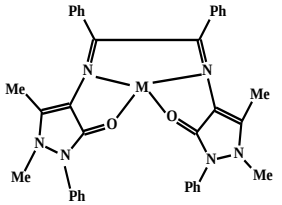
Schiff bases are identified as promising antibacterial agents. For example, N-(Salicylidene)-2-hydroxyaniline is active against Mycobacterium tuberculosis [69].



The in vitro screening of biocidal potential of the schiff base ligand (DE) Scheme Z and its vanadyl and uranyl complexes as antibacterial, antifungal and antihelminthic agents was investigated. The antibacterial activity of the ligand (DE) and its metal complexes towards the gram postive bacteria S.aureus, and the gram negative bacteria *K. penumoniae*, *S. typhi*, *E.coli* and *S. flxneri* were compared through the radius of inhibition zone against Gentamycin (control). The study reveals that antibacterial activity increase with complexation [70]. The antibacterial, antifungal and antihelminthic activities were found to be in the order [VODE] SO4 > [UO2DE] (NO3)2 > (DE).

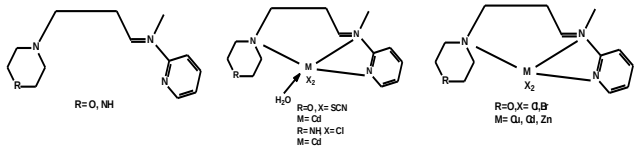


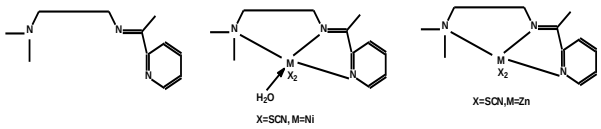
(DE)



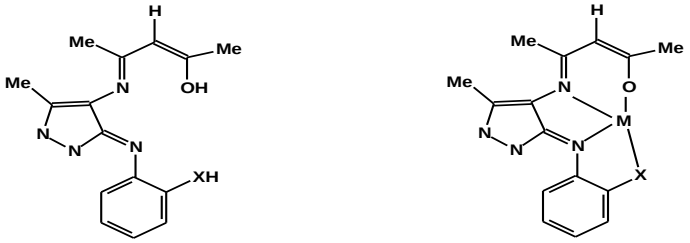
M= UO_2^{2+}, VO^{2+}

A series of schiff bases derived from 2-acetyl pyridine and their metal complexes of Cu(II), Cd(II), Zn(II), Ni(II), were screened for their antibacterial activity against Methicillin-resistant *Staphylococcus aureus*(MRSA), *Acinetobacter baumanni*, *Klebsiella pneumonie* and *Pseudomonas aeruginosa*. The complexes showed the highest activity against (MRSA) and weak activities against *A. baumanni*, and *Pseudomonas aeruginosa* was observed [71].



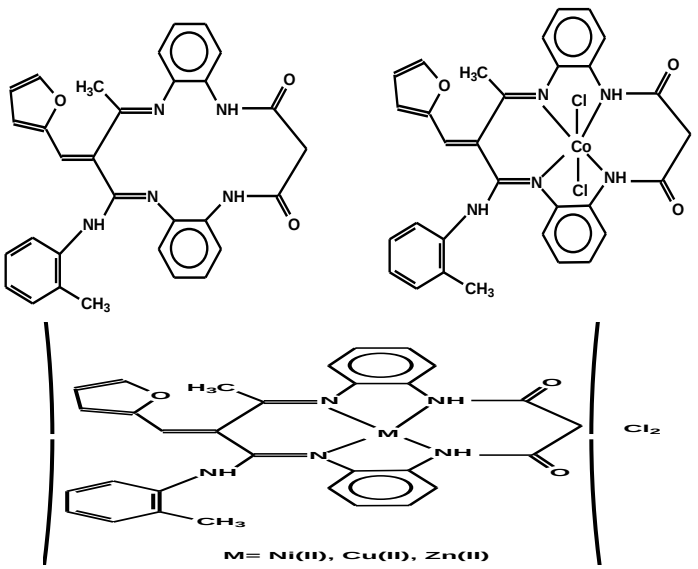


Neutral tetradentate complexes of transition metals with Schiff bases derived from 2- aminophenol/2-aminothiophenol and 1-phenyl-2,3- dimethyl-4(4-iminopentan-2-one)-pyrazol-5-one showed antimicrobial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella imeumoniae*, *Salmonella typhi*, *Pseudomonous aeruginosa*, *Shigella flexneri*, *Aspergillus niger* and *Trichoderma viridi*. Most of the complexes have higher activity than the free ligand [72].

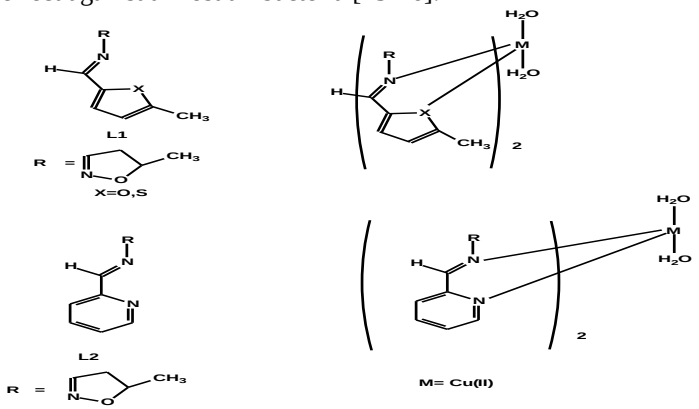


H2L1 ,X=O H2L2, X=S M= Cu, Ni, Co, Zn

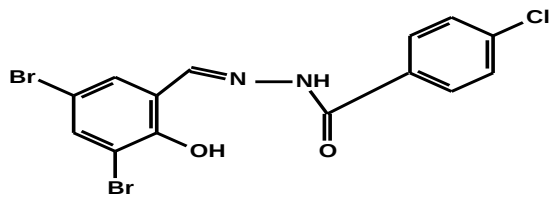
Tetradentate Schiff base ligands derived from condensation of β-ketoanilides and furfural with o-phenylenediamine and diethylmalonate and their Cu (II),Ni(II), Co(II), Zn(II) complexes showed antibacterial activity against *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* by disc diffusion method. It has been reported that complexes have higher antibacterial activity than that of free ligand [73-74].



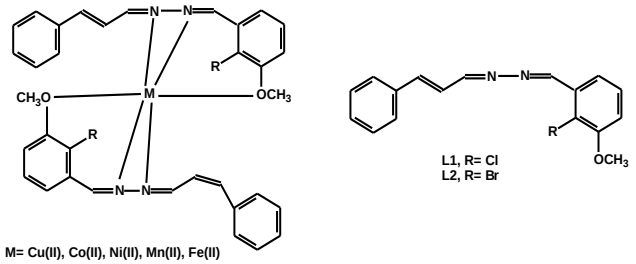
Bidentate Complexes of Cu (II) with Schiff bases derived from 2,6-diacetylpyridine (L1), 2-pyridine carboxaldehyde, 3-amino-5-methyl isoxazole with 5-methyl furan-2-carboxyaldehyde, 5-methyl thiphene-2-carboxaldehyde and pyridine-2-carboxaldehyde coordinate through the azomethine nitrogen, furfural oxygen, thiophene sulphur and pyridine nitrogen, respectively show antibacterial activity against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Mycobacterium Smegmatis, Pseudomonas aeruginosa, Enterococcus cloacae, Bacillus megaterium* and *Micrococcus leteus.* The results showed that L_1 ligand has a greater effect against *E. coli* than the other bacteria, while it has no activity against *S. aureus*. Metal complexes have a greater effect against almost all bacteria [75-76].



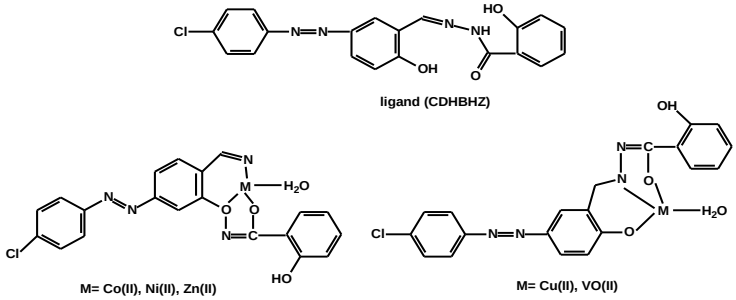
Schiff base of aroyl-hydrazone ligand L and its copper complexes has been screened for antibacterial activity against two Gram positive bacterial strains (B. subtilis and S. aureus) and two Gram-negative bacterial strains (*E. coli* and *P. fluorescence*) by the (MICs) method. Schiff base showed significant activity against two Gram-negative bacterial strains with MIC but inactive against two Gram positive bacterial strains [77].



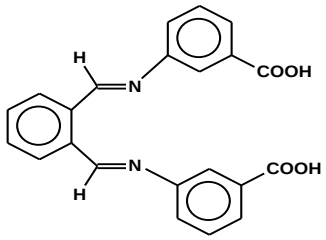
tetradentate Schiff base complex derived from the condensation of Cinnamaldehyde hydrazone with different benzaldehyde Cu (II), Co (II), Ni (II), Mn(II) and Fe(II) complexes screened more active against gram positive bacteria *Bacillus subtilis* than gram negative bacteria *E. Coli*[78].



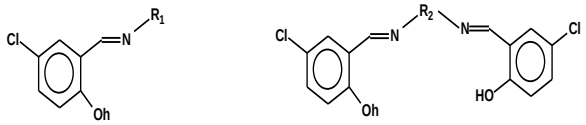
Azo Schiff's base ligand (N′E)-N′-(5-((4-chlorophenyl) diazenyl)-2-hydroxybenzylidene)-2-hydroxyl benzohydrazide and its complexes with VO (II), Co (II), Ni (II), Cu (II), and Zn (II) (Scheme yx) has been studied against several microorganisms by the well diffusion method. In general, the activity order of the synthesized compounds can be represented as Cu (II) > Co (II) > Ni (II) > Zn (II) > VO (II) > Ligand [79].



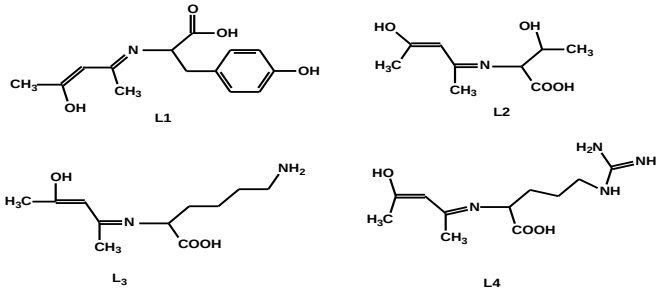
Tetradentate schiff base and their complexes of Cu(II) and Fe(III) show antibacterial activity comparable to that of standard drugs[80].



A number of schiff bases derived from 5- chloro-salicylaldehyde were studied for their anti bacterial and anti fungal activities. They show significant antibacterial activity with very low antifungal activities [81].

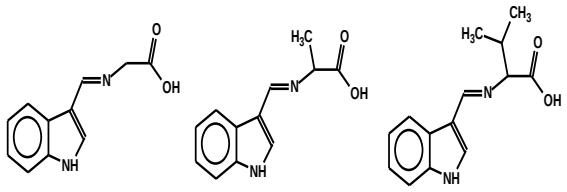


A series of amino acid derived schif bases and their oxovanadium (IV) complexes [82] were screened for their in vitro anti bacterial activity against *E.coli , S. typhi*(Gram-negative) and *B. subtilis, S. aureus*(Gram – positive),the result revealed that all the compounds and their complexes showed significant antibacterial and antifungal activities.

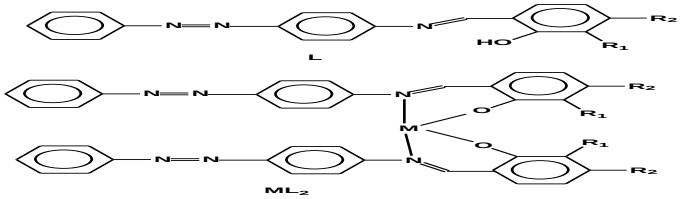


$M(L)(H_2O)$ M= VO, L= L_1, L_2, L_3, L_4

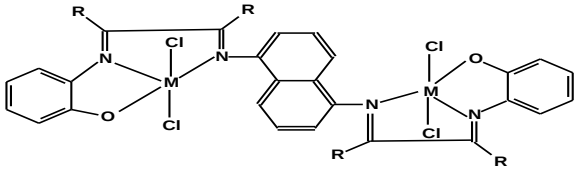
The antibacterial activity of amino acid schiff bases was reported against S. aureus, E. coli and B. subtilis, it was found that all compounds are active against the tested microorganisims [83]. The activities of schiff bases may be due to the presence of carboxyl group [84]



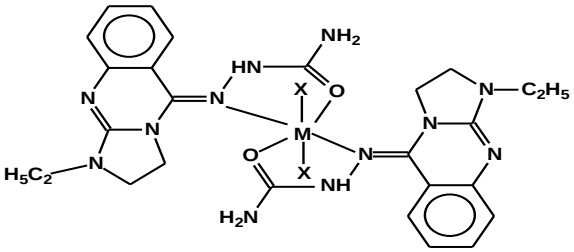
Some novel azo containing schiff bases ligands and their complexes of Co(II), and Cu(II), were tested for antimicrobial activity. Ligands did not show any activity while the metal complexes show good antimicrobial activity [85].



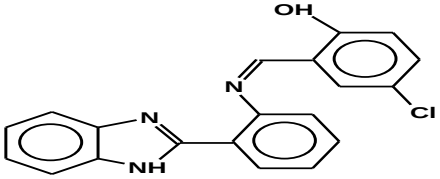
The Schiff bases and their complexes have been screened for their in vitro antibacterial activity against various bacteria, by paper disc method, it result confirms the binuclear complexes are more potent than free ligands [86].



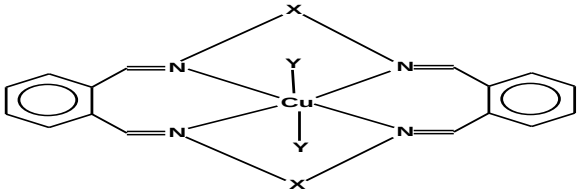
A series of transition metal complexes (M = Co(II), Ni(II), and Cu(II), X = Cl^-, Br^-, NO_3-) with Schiff base ligand 1-ethyl,1,2,3,5,tetrahydroimidazo(2,1-b)quinazolin5-one semicarbazone have been synthesized. All synthesized ligand and complexes have been screened for antimicrobial activity. The metal complexes are more potent than the free ligand [87].



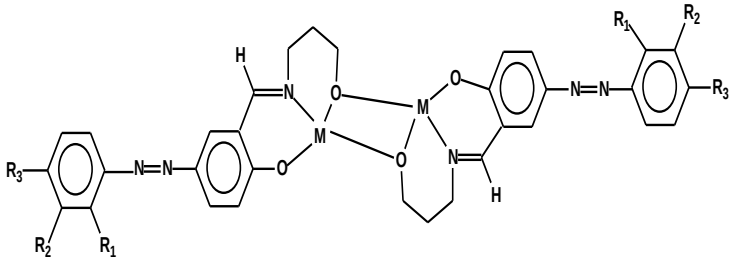
A series of Ni(II), Co(II), Cu(II), and VO(IV) complexes have been synthesized from the Schiff base ligand (2-[(Z)-{(2-(1H-Benzimidazole- 2yl)phenyl]imino}methyl]–4-chlorophenol (BMCP). All the complexes were tested for their antibacterial activity. Antimicrobial activity of the ligand and its metal complexes were studied against two gram negative, and two gram positive bacteria. The activity data show that the metal complexes are more potent than the free ligand [88].



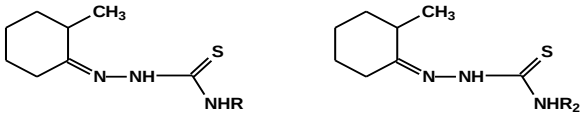
Novel family of tetraaza macrocyclic Cu(II) complexes [CuLX2] (where L = N_4 donormacrocyclic ligands) and (X = Cl^-, NO_3^-) have been synthesized. The antibacterial activity of all these complexes against Gram positive and Gram negative bacteria was compared with the activity of existing commercial antibacterial compounds. The complexes were found to be most potent against both Gram positive as well as Gram negative bacteria due to the presence of thio group in the coordinated ligands [89].



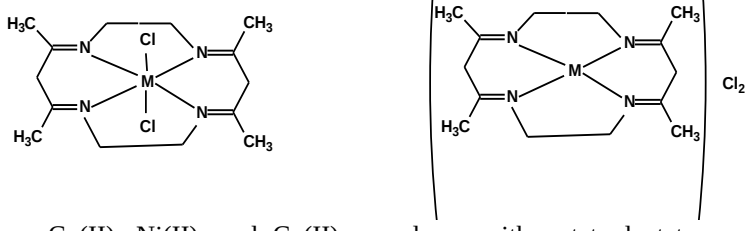
Azo group-containing Schiff base ligands, and their metal complexes (M = Cu (II) and Co(II)) were synthesized. Ligands and all the complexes were tested for their antibacterial activity. The results indicate that the ligands have some activity against the bacteria. The complexes have more activity than ligand [90].



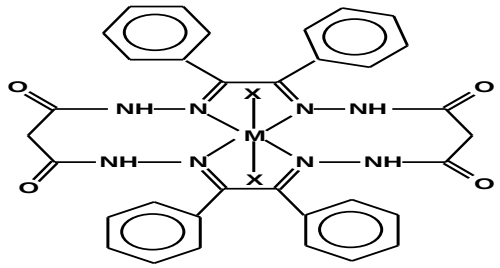
New Co(II) and Ni(II) complexes of 4Nsubstituted thiosemicarbazones derivatives of 2-methylcyclohexanone of general composition ML_2X_2 where M = Co(II), and Ni(II), X = Cl^-, SCN^-, and SO_4^{2-}. Thiosemicarbazones exist in thione form and coordinate to metal ion through sulphur atom of C, S group and azomethine nitrogen. The complexes and ligands have also been tested in vitro for their antifungal activity. The experimental results suggest that metal chelates are more active than parent ligands [91].



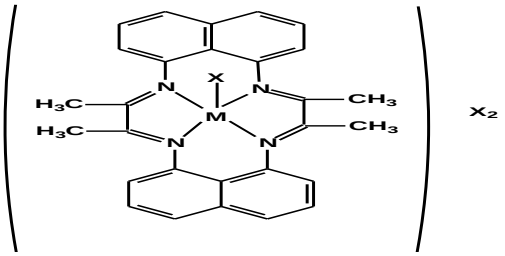
Metal complexes (M = Mn(II), Co(II), Ni(II), Pd(II), and Pt(II)) of tetradentate macrocyclic nitrogen ligand i.e. 1,5,8,12-tetraaza- 2,4,9,11-tetramethyl cyclotetraaza-1,4,8,11- tetraene, have been synthesized. In vitro the ligand and its complexes were tested against two pathogenic fungi to assess their growth inhibiting potential [92].



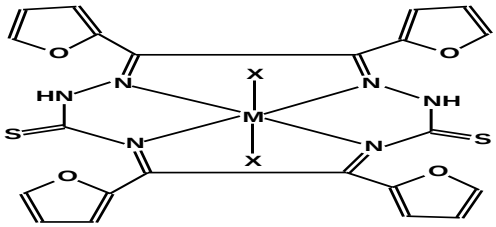
Co(II), Ni(II), and Cu(II) complexes with a tetradentate nitrogen donor [N_4] macrocyclic ligand, 6,15-dimethyl-8,17diphenyl-7,16 dihydrodibenzo[b,i][1.4.8.11] tetraazacyclotetradecine, were synthesized. All the complexes have been screened for their in vitro antifungal activity. The compounds exhibit significant antifungal activity [93].



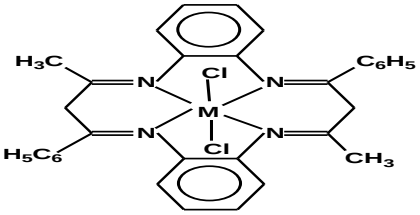
A novel series of complexes of the type [M(C28H24N4)X]X2, where M = Cr(III), Fe(III), and Mn(III), X = Cl−, NO_3 −, OAc− and (C28H24N4) corresponds to the tetradentate macrocyclic ligand, have synthesized by condensation of 1,8-diaminonaphthalene and 2,3-butanedione(diacetyl) in the presence of metal salts. All the complexes were tested for their in vitro antifungal activity against some fungal strains. The results obtained were compared with the standard antifungal drug [94].



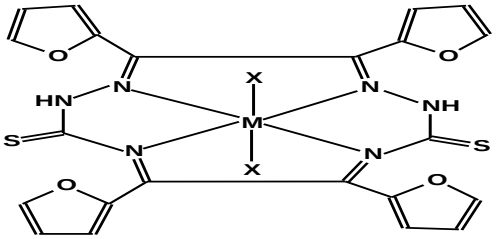
New complexes of 12-membered macrocyclic Schiff base ligand containing thiosemicarbazone moiety have been prepared of general composition [MLX_2] where M = Mn(II) and Cu(II), L = 3,4,9,10–tetra-2-furanyl-1,2,5,6,8,11- hexaazacyclododeca-7, 12-dithione-2,4,8,10– tetraene, X = Cl-, NO3 - and NCS-. All the examined complexes have also been tested in vitro against a number of pathogenic fungi. Results indicated that the complexes exhibited good antifungal activities [95].



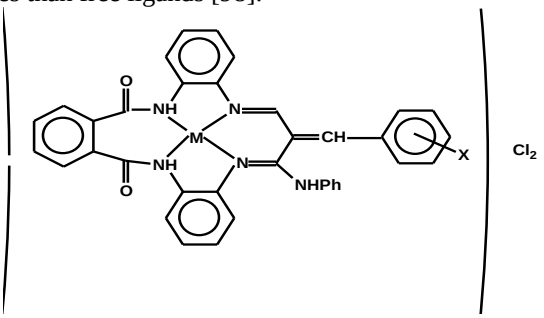
Co(II), Ni(II), and Cu(II) complexes with a tetradentate macrocyclic ligand, 6,15-dimethyl- 8,17diphenyl-7,16 dihydrodibenzo[b,i][1.4.8.11]tetraazacyclotetradecine, were synthesized. The ligand and its complexes were screened for fungicidal activity against two pathogenic fungi to assess their growth inhibiting potential [96].



New Co(II) and Ni(II) complexes of 12- membered macrocyclic Schiff base ligand containing´thiosemicarbazone moiety as a part of ring have been prepared having general composition [MLX2] where M=Co(II), and Ni(II), L=3,4,9,10–tetra-2-furanyl-1,2,5,6,8,11- hexaazacyclododeca-7,12- dithione -2,4,8,10 – tetraene, X = Cl-, NO3 -, NCS. The antifungal activities of complexes have been studied against a number of pathogenic fungi. The complexes showed good antifungal results [97].



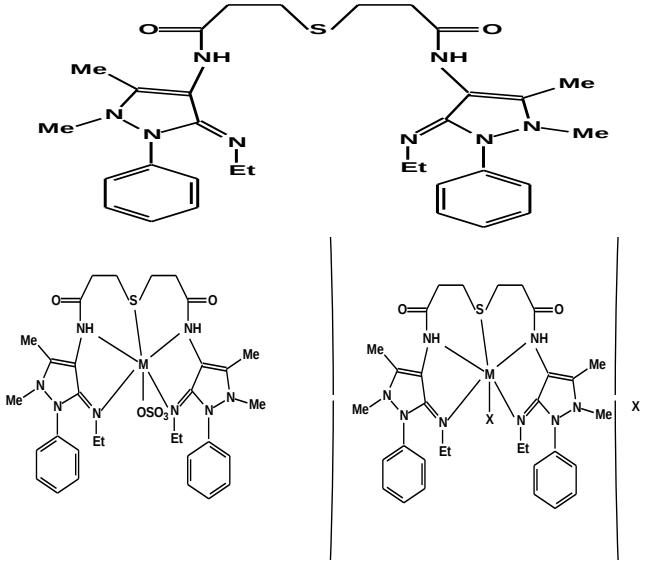
The macrocyclic ligands have been synthesized by the condensation reaction ofdiethyl phthalate with Schiff bases derived from o-phenylenediamine and Knoevenagel condensed β- ketoanilides. The antifungal activities of the compounds were tested against fungi. All complexes showed stronger antifungal activities than free ligands [98].



The microbial activity of the N-(2-hydroxy-1-naphthalidene) phenylglycine and its transition metal complexes was investigated. From the antifungal screening data it is concluded that the activity of the ligand has increased upon complexation. Cu(II), Ni(II) and Co(II) complexes have shown better antifungal activity compared to the ligand and the corresponding metal salts[99]. Two bidentate Schiff base ligands 2- (2-hydroxy-3, 5-dichloro/dibromo) benzaldehyde-[4- (3-methyl-3-mesitylcyclobutyl)-1, 3-thiazol-2- yl]hydrazone, L1H, L2H and their metal complexes were tested against a yeast-like fungus *C.albicans*[100]. The fungicidal effect of salicylaldimine containing formaldehyde and piperazine moity and its metal polychelates were determind against two yeast *Candida albicans*, *Aspergillus niger*. The Cu(II)-polychelate exhibited high activity against Candida albicans and the other show mild activity. The presence of N and O donor groups in the ligand and its metal polychelates inhibited enzyme production because enzymes that require free hydroxyl group for their activity appear to be especially susceptible to deactivation by the metal ion of polychelates. All the metal polychelates are more toxic than the ligand[101]. Neutral complexes of Co(II), Ni(II), Cu(II) and Zn(II) with Schiff bases derived from 3-nitrobenzylidene-4-aminoanttipyrine and aniline(L1)/p-nitroaniline(L2)/p-methoxyaniline (L3) showed antifungal activity. A comparative study of the MIC values for the ligands and their complexes indicates that the complexes exhibit higher antimicrobial activity. Such increased activity of the complexes can be explained on the basis of overtone's concept and chelation theory[102]. Inhibition is enhanced with the introduction of an electron withdrawing nitro group in the phenyl ring[103]. Semicarbazones and thiosemicarbazones complexes of Ni(II) metal showed antifungal activities against 11 pathogenic fungi. The complexes were moderate active against all pathogenic fungi and much lower than those of standard fungicide Nistatin[104].

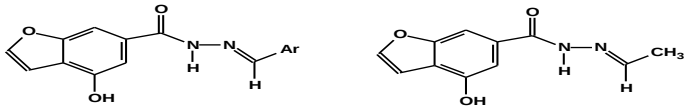
Co(II),Ni(II) and Cu(II) complexes with Schiff base 3,3'-thiodipropionic acid bis(4-amino-5-ethylimino-2,3-dimethyl-1-phenyl- 3-pyrazoline showed antifungal activity against

Alternaria brassicae, Aspergillus niger and *Fusarium* oxysprum and results indicate that the complexes show the enhanced activity in comparison to free ligand[105].



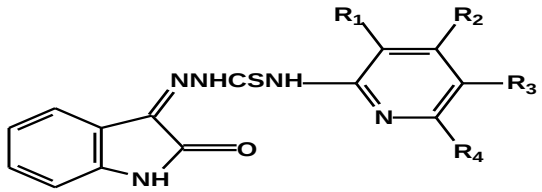
M= Co(II), Ni(II), Cu(II)
X= NO3-, Cl-, OAc-

Synthesis and pharmacological studies of novel schiff bases of 4-Hydroxy 6-carboxyhydrazino benzofuran was reported [106]

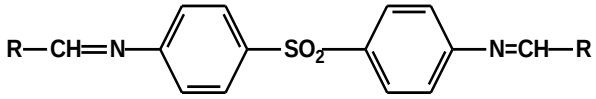


The microbial activity of the N-(2-hydroxy-1-naphthalidene)phenylglycine and its transition metal complexes was investigated. From the antifungal screening data it is concluded that the activity of the ligand has increased upon complexation. Cu(II), Ni(II) and Co(II) complexes have shown better antifungal activity compared to the ligand and the corresponding metal salts[99].

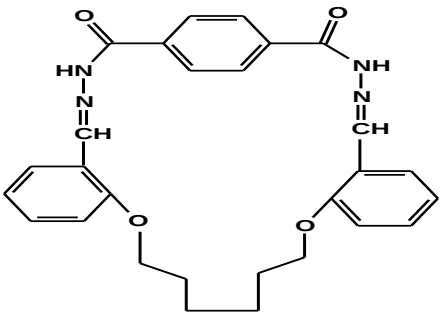
Vijey Aanandhi [107] reported the synthesis of a series of 1-(5-substituted-2-oxoindolin-3-ylidene)- 4-(substituted-pyridin-2-yl)thiosemicarbazide derivatives. These compounds were screened for in vitro antibacterial and antifungal activity against *B.subtilis ,S. aureus, E.coli, P. aeruginosa, C. albicans,* and *A. niger*. All the compounds were reported to exhibit moderate to good antibacterial and antifungal activity.



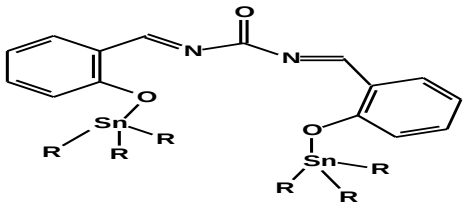
Aseries of schiff bases derived from 4,4`-diaminodiphenylsulphone and several aromatic aldehydes. The schiff bases exhibit potent antibacterial activity compared to that of the standard ciprofloxacin [108].



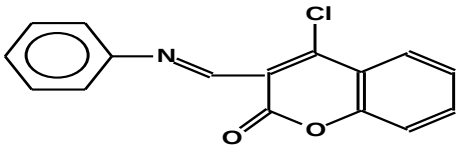
New macrocyclic hydrazone schiff bases were studied for antibacterial activity against B.Subtilis, S. aureus, S.typhi and E. coli. The compounds show variable antibacterial activities[109].



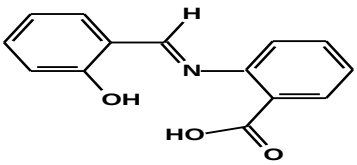
Jamil and coworkers have reported the synthesis and antimicrobial activities of novel organotin schiff bases [110].



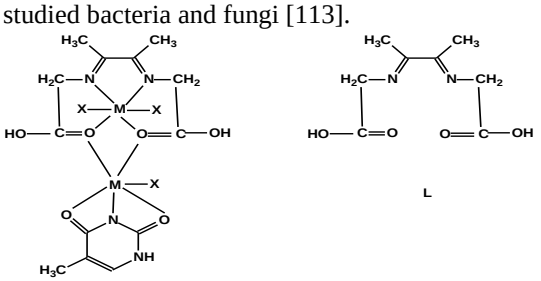
4-chloro-2-oxo-2H-chromene-3-carbaldehyde when reacted with anilines, schiff bases were obtained. The schiff bases compounds were screened for their antibacterial and antifungal activities [111].



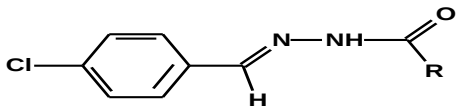
Preparation, physical characterization and antibacterial activity of Ni (II) Sciffbase complex was reported by Morad et al [112].



Novel binuclear metal complexes of general formula [M2(PymL)X3] (where: M= Cu(II), Ni(II), Co(II) or Zn(II); X= Cl_ or CH3CO2_ and PymL =C13H17N4O6) were synthesized by template condensation of Schiff base (L) derived from glycine using 2,3-butanedione, 5- methyl-2,6-pyrimidine-dione and metal chloride/acetate salt in 1:1:2 stoichiometric ratio. Synthesized. The compounds were evaluated for their antimicrobial property by in vitro antimicrobial screening against bacteria *Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Salmonella typhi* and fungi *Candida albicans* and *Candida parapsilosis.* The results indicate that metal complexes exhibit more activity than free Schiff base (L) against studied bacteria and fungi [113].



Schiff bases derived from 4-chlorobenzaldehyde and substituted hydrazide were investigated for antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Salmonella typhi* [114].



Conclusion

With proper design and structure activity relationship of schiff bases, prospective compounds with a very good biological activity can be prepared together with their transition metal complexes, which they appear to be future medicinal candidates.

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