Review Article www.ijcps.com

International Journal of Chemical and Pharmaceutical Sciences
2014, June., Vol. 5 (2)

ISSN: 0976-9390
IJCPS

Antibacterial and antifungal activity of Schiff base ligands and their metal complexes-A Review

Sulekh Chandra* and Seema Gautam

Department of Chemistry, Zakir Husain College, University of Delhi, J.L. Nehru Marg, New Delhi, India.

* **Corresponding Author:** E-Mail: Schandra_00@yahoo.com

ABSTRACT

Schiff base ligands and their metal complexes are very important in medicinal and pharmaceutical fields because of their wide spectrum of biological activities. This review describes antibacterial and antifungal activities on the coordination chemistry of multidentate open chain and macrocyclic Schiff base ligands and their metal complexes. These promising results are encouraging further for inorganic as well as bio-inorganic chemists.

Keywords: Coordination chemistry, Open and macrocyclic, Schiff base, Ligand, Metal complexes, Antibacterial, Antifungal activity.

1. INTRODUCTION

Coordination chemistry, widely developed in the last few decades, is highly considered in inorganic, organic and biological fields [1-4]. Coordination chemistry has always been a challenge to the chemists as it has more branches now-a-days. [5-10] In coordination chemistry, Schiff base ligands, which can be synthesized from the condensation of primary amines with carbonyl compounds (Figure 1) play an important role.

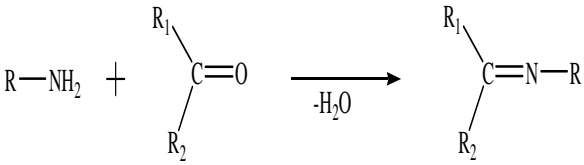


Figure - 1: Formation of Schiff base by condensation reaction (R group may be various substitute)

Schiff base ligands regarded as "privileged ligands" received a great attention because they are able to coordinate metals through imine nitrogen and another group usually linked to aldehyde or ketone [5]. Not only they have played a role in the development of coordination chemistry, but they can also be found at key points in the development of inorganic biochemistry. [6-8] These 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. [9-11] It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities. [12,13] Schiff bases and their metal complexes have wide applications in food industry, dye industry, analytical chemistry, catalysis, agrochemical, and biological field. [14-16] A stable open and macrocyclic Schiff base ligands and their metal complexes have become the most well known of all metal based drugs. [17-20] More than thousands of articles have been published on the synthesis and biological activities of Schiff base metal complexes, [21-23] such as chromium, manganese, cobalt, iron, calcium, lanthanum, nickel, and copper. [24-32] More recently, these ligands and their metal complexes have been found to possess antiviral, [33] antitumor [34] antioxidant, [35] DNA binding and DNA cleavage, antibacterial and antifungal activities. This review highlights extensive studies on syntheses, and the antibacterial and antifungal activities of open chain and macrocyclic Schiff-base ligands (mono and polydentate) and their metal complexes. The present review updated these results.

2. ANTIBACTERIAL ACTIVITIES

The increase in the mortality rate associated with infectious diseases is directly related to bacteria that exhibit multiple resistances to antibiotics. The lack of effective treatments is the main cause of this problem. The development of new antibacterial agents with novel and more efficient mechanisms of action is definitely an urgent medical need. Schiff bases have been pointed to as promising antibacterial agents.

A series of Schiff base metal complexes (M = Cu(II), Co(II), and Ni(II) have been synthesized with Schiff base derived from 1,5-diaminonaphthalene, glyoxal/ biacetyl and 2-

aminophenol (Figure 2). 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 [36].

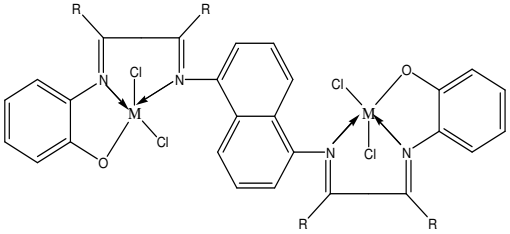


Figure - 2.

The 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 (Figure 3) have been synthesized. All synthesized ligand and complexes have been screened for antimicrobial activity. The metal complexes are more potent than the free ligand [37].

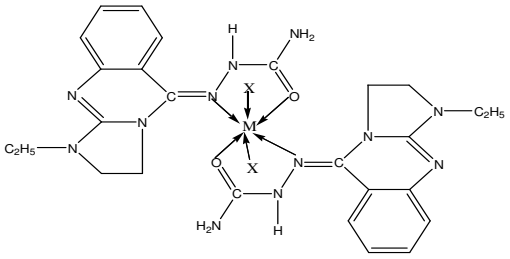


Figure - 3.

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) (Figure 4). 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 [38].

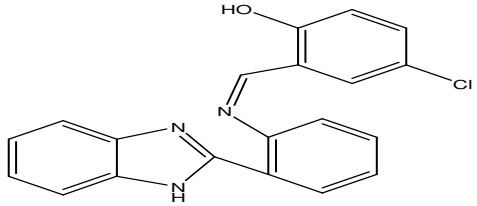


Figure - 4.

A novel family of tetraaza macrocyclic Cu(II) complexes [$CuLX_2$] (where L = N_4 donor macrocyclic ligands) and (X = Cl^-, NO_3^-) have been synthesized (Figure 5). 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 [39].

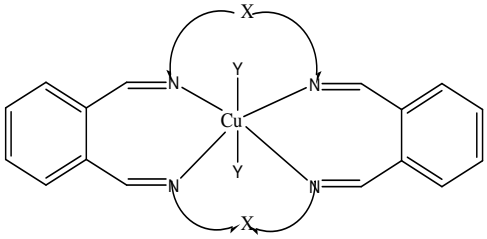


Figure - 5.

Azo group-containing Schiff base ligands, and their metal complexes (M = Cu(II) and Co(II)) were synthesized (Figure 6). 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 [40]**.**

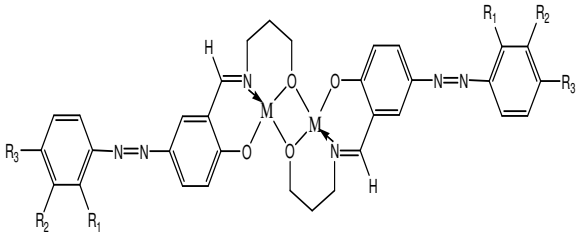


Figure - 6.

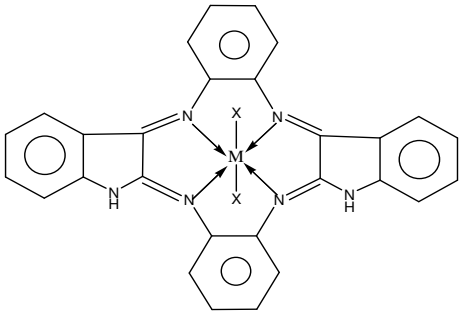


Figure - 7.

A novel series of complexes of the type [$M(C_{28}H_{18}N_6)X_2$], where M = Co(II), Ni(II), Cu(II), and Zn(II) and X = Cl^-, NO_3^-, OAc^-, were synthesized by template condensation of isatin and 1,2-diaminobenzene in methanolic medium (Figure 7). All the synthesized macrocyclic complexes were also tested for their *in vitro* antibacterial activity against some pathogenic bacterial strains. The *MIC* values shown by the complexes against these bacterial strains were compared with standard antibiotics. Some of the complexes showed good antibacterial activities [41].

New tetradentate N_2O_2 donor Schiff bases and their metal complexes (M = Co(II), Ni(II), Cu(II), Pd(II)) were synthesized (Figure 8). All the ligands and complexes were screened for their *in vitro* antibacterial activity against two gram positive and two gram negative bacteria. In this study, Pd(II) complexes exhibited potent antibacterial activity against *B. subtilis*, *S. aureus* whereas other metal complexes also show more activity towards all tested strains than standard drugs [42].

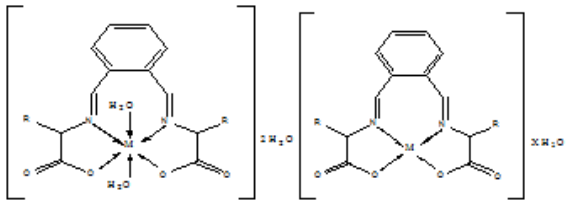


Figure - 8.

New (Z)-2-(pyrrolidin-2-ylidene)hydrazinecarbothioamide (L) was synthesized in a good yield by the reaction of pyrrolidone with thiosemicarbazide. Metal complexes (M = Co(II), Ni(II), Cu(II)) of (L) were prepared (Figure 9). The free ligand and its metal complexes were tested *in vitro* against several microorganisms to assess their antimicrobial properties. The study shows that these complexes have high activity against tested bacteria [43].

A new series of macrocyclic metal complexes (M = Cu(II), Ni(II), VO(IV) and X = ClO_4^-) have been prepared (Figure 10). Schiff base ligand has been synthesized from freshly prepared O-aminobenzaldehyde and benzidine. This synthesised ligand reacts with 2,3-pentanedione and metal salts to form a macrocyclic binuclear Schiff base complexes. The parent Schiff base and its complexes are assayed against gram negative bacteria like *Klebsiella pneumoniae, Escherichia coli* and gram positive bacteria like *staphylococcus aureus* by disc diffusion technique. The inhibition of bacterial growth high at Cu(II) complex [44].

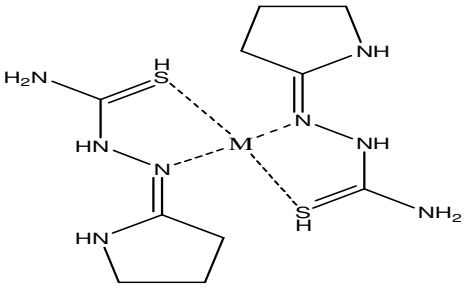


Figure - 9.

Complexes of Ni(II) of N,N'-disalicylidene-3,4-diaminotoluene(a), N,N'-bis(3,5-di-tertbutylsalicylidene)-1,3-diaminopropane(b),tetrathiafulvalene-N,N' phenylene bis(salicylideneimine)(c), o-hydroxybenzaldehyde, o-hydroxyacetophenone ethylenediamine (d) and 1-phenylbutane-1,3-dionemono-S-methylisothio-semicarbazone with 5-phenylazo- ohydroxybenzaldehyde (e) have been synthesized (Figure 11). The bio-efficacy of the ligands and their complexes has been examined against the growth of bacteria *in vitro* to evaluate their antimicrobial potential [45].

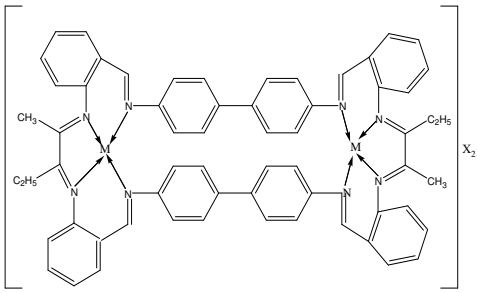


Figure - 10.

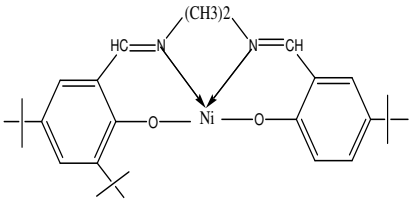


Figure - 11(a)

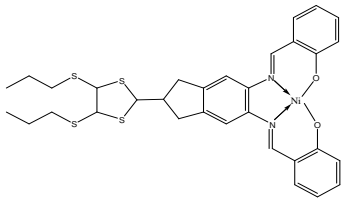


Figure – 11(b)

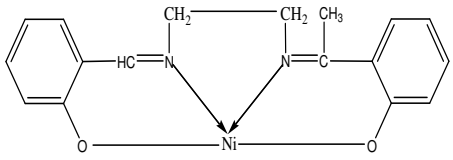


Figure – 11(c)

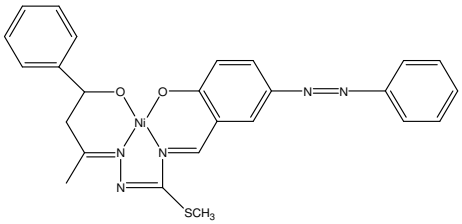


Figure – 11(d)

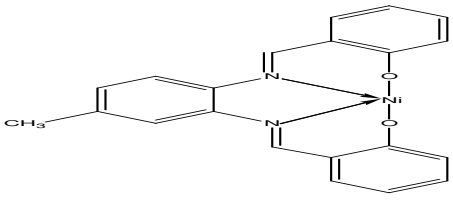


Figure – 11(e)

Macrocyclic Schiff base ligand is prepared via condensation of 2,6-pyridine dicarboxaldehyde with triethylenetetramine. Metal complexes (M = Cr(III), Fe(III), Co(II), Ni(II), Cu(II), Cd(II) X = Cl^-) have been synthesized (Figure 12). The parent Schiff base and its eight metal complexes were assayed against four bacterial species, two gram negative, and two gram positive. The Schiff base and five of its metal complexes showed antibacterial activity at different rates. The complexes of Cr(III) and Cu(II) inhibited gram positive bacteria, while Co(II) complex inhibited all tested bacteria greater than the parent Schiff base [46].

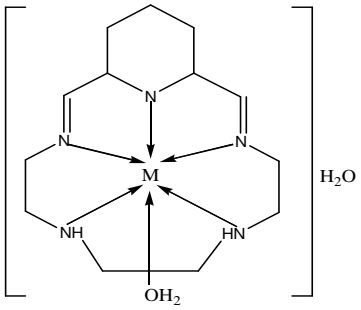


Figure - 12.

Tetraaza Macrocyclic complexes of transition metals of Ni(II), Cu(II), Cr(III), Fe(III), and Mn(II) were synthesized in methanolic media by template method (Figure 13). *In vitro* antibacterial activity of macrocyclic complexes against five pathogenic bacterial strains were tested to assess their inhibiting activities and compared with standard drug [47].

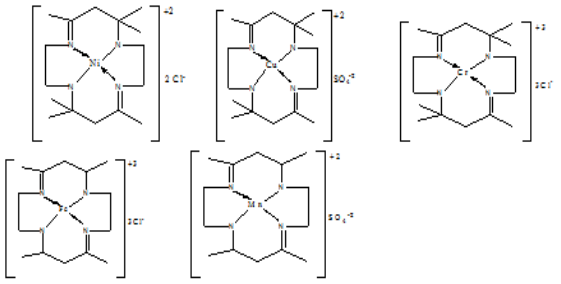


Figure - 13.

The new complexes $M(DMBG)_2(ClO_4)_2$ (M = Mn(II), Ni(II), Cu(II), and Zn(II) DMBG = N,N-dimethylbiguanide) have been synthesized (Figure 14). The metal-free N,N-dimethylbiguanide and complexes exhibit specific anti infective properties as demonstrated the low MIC values, a large antimicrobial spectrum and also inhibit the ability of *Pseudomonas aeruginosa* and *Staphylococcus aureus* strains to colonize the inert surfaces [48].

A new asymmetric heptaaza Schiff base macrocyclic bis(pendant donor) Mn(II) complex, has been prepared (Figure 15). The antimicrobial activity of pendant armed Schiff base macrocyclic complexes of Mn(II) were tested against pathogenic bacterial strains. The results showed that the symmetric heptaaza Schiff base macrocyclic complexes of Mn(II) had remarkable inhibition zone on the culture of *S. aureus and E. Coli* as compared with standard drugs [49].

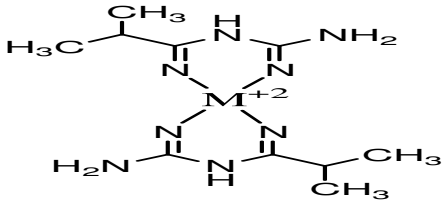


Figure - 14.

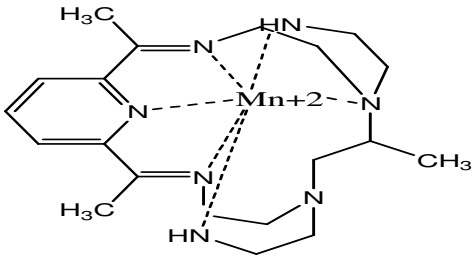


Figure - 15.

The new macrocyclic Schiff base ligands were synthesized by the condensation reaction between 9,10-phenanthrenequinone and *o*-phenylenediamine. The ligands react with vanadylsulphate to form metal complex (Figure 16). Further the complexes have been subjected to antimicrobial activity [50].

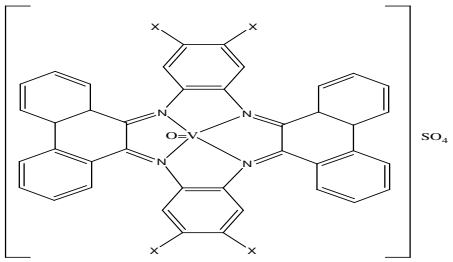


Figure - 16.

The macrocyclic ligands are synthesized by condensation of o-phenylenediamine and 4-4diamino, diphenyl methane with acetyl acetone in ethanolic medium followed by formation of their complexes with vanadium salt (Figure 17). The biological activities of all compounds have been studied by screening them against organism gram negative, and gram positive bactria [51].

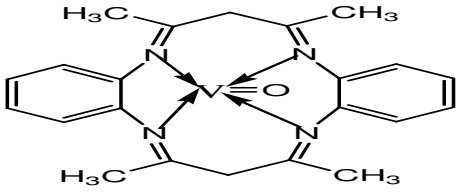


Figure - 17.

A new series of macrocyclic complexes, $[M(C_{48}H_{32}N_4)X_2]$, where M = Co(II), Ni(II), Cu(II), and Zn(II), X = Cl^-,NO_3^-, OAc^-, have been synthesized by condensation of 1,8-diaminonaphthalene and benzil, in the presence of divalent metal salts (Figure 18). The metal complexes were also tested for their in vitro antibacterial activities against some bacterial strains and compared with the standard antibiotic. Some tested complexes show good antibacterial activities against some bacterial strains [52].

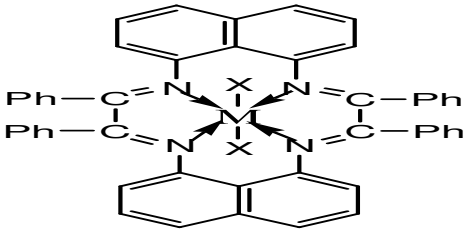


Figure - 18.

Some metal complexes, ML_2 [M = Co(II), Ni(II), Cu(II) and Zn(II)], of 2-acetylthiophene benzoylhydrazone ligand (L) containing a tri functional SNO-donor system have been synthesized (Figure 19). The complexes showed remarkable antibacterial activities against some selected bacterial strains [53].

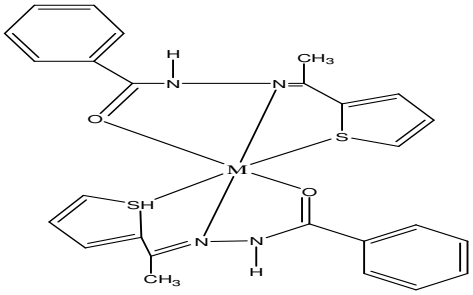


Figure - 19.

The condensation reaction of succinyldihydrazide with glyoxal in the presence of divalent metal ions results in the formation of the complexes of type $[M(C_6H_8N_4O_2)X_2]$, where M = Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) and X = Cl^-, NO_3^-, OAc^- (Figure 20). The complexes were tested for their in vitro antibacterial activity. Some of the complexes showed remarkable antibacterial activities against some selected bacterial strains [54].

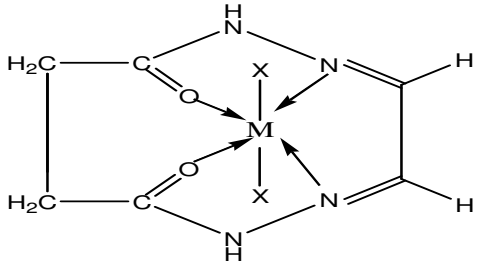


Figure - 20.

A novel series of the complexes of the type $[M(TML)X]X_2$, where TML is a tetradentate macrocyclic ligand, M = Cr(III), and Fe(III), X= Cl^-, NO_3^-, OAc^- have been synthesized by condensation of indole-2,3-dione (isatin) and o-phenylenediamine (Figure 21). The complexes were also tested for their *in vitro* antibacterial activities. Some of the complexes showed remarkable antibacterial activities against some of the selected bacterial strains [55].

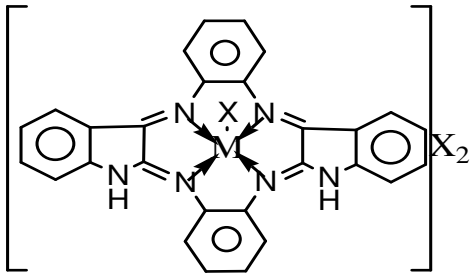


Figure - 21.

Novel Schiff base ligand via condensation of benzil and triethylenetetraamine and metal complexes (M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) and X = Cl^-) have been synthesized (Figure 22). The ligand, in comparison to its metal complexes, is screened for its antibacterial activity. The activity data show that the metal complexes have antibacterial activity more than the parent Schiff base ligand and standard against one or more bacterial species [56].

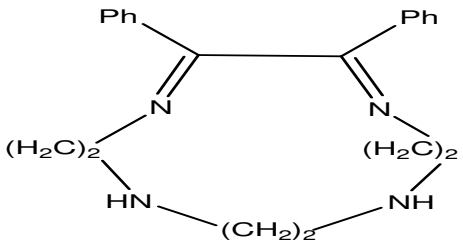


Figure - 22.

A new Schiff base 2-aminophenol-pyrrole-2-carboxaldehyde and its metal complexes (M = Zn(II), Cd(II), Sn(II) and Pb(II) and X =Cl^-, NO_3^-, OAc^-) have been synthesized (Figure 23). The bio-efficacy of the ligand and their complexes has been examined against the growth of bacteria in vitro to evaluate their antimicrobial potential [57].

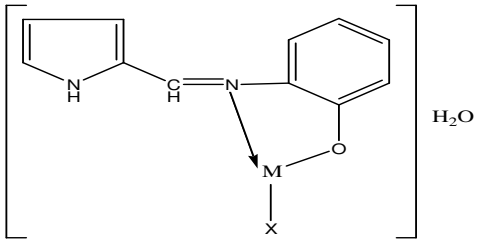


Figure - 23.

A novel series of complexes of the type $[M(C_{28}H_{24}N_4)X_2]$, where M = Co(II), Ni(II), Cu(II), Zn(II) and Cd(II), X = Cl^-, NO_3^-, OAc^- corresponds to the tetradentate macrocyclic ligand, were synthesized (Figure 24). All macrocyclic complexes were tested for *in vitro* antibacterial activity against some pathogenic bacterial strains. The *MIC* values shown by the complexes against these bacterial strains were compared with the *MIC* shown by the standard antibiotics [58].

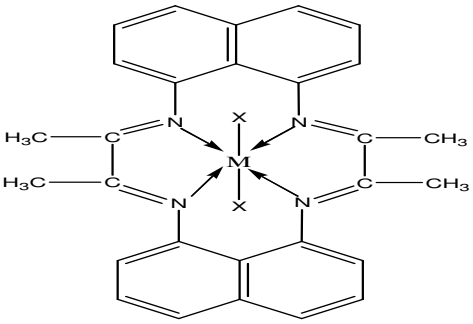


Figure - 24.

A series of N,N′-bis(2-hydroxylbenzyl)-1,2-ethanediamine derivatives and its Schiff bases were synthesized (Figure 25), and screened for *in vitro* antimicrobial activity against pathogenic bacterial strains [59].

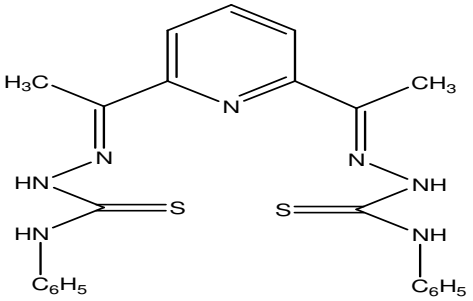
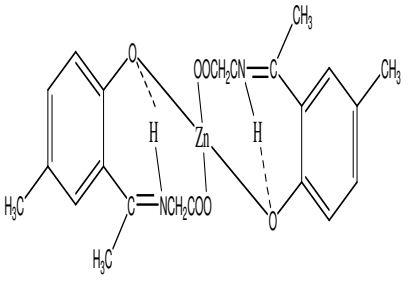


Figure - 25.

Synthesis of a new Schiff base derived from 2-hydroxy-5-methylacetophenone and glycine and its complexes Co(II), Ni(II), Cu(II), Zn(II), UO_2(VI) have been synthesized (Figure 26). Antibacterial activities of ligand and its metal complexes have been determined by screening the compounds against various gram and gram bacterial strains [60].



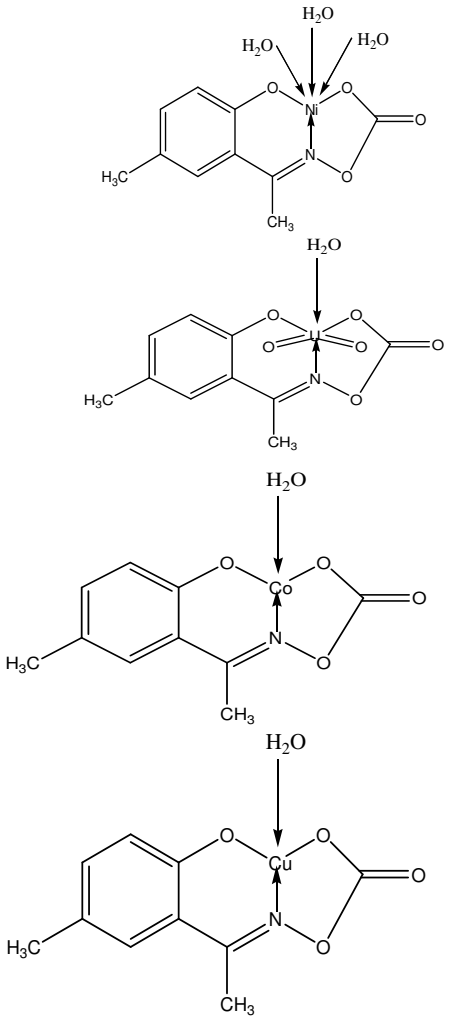
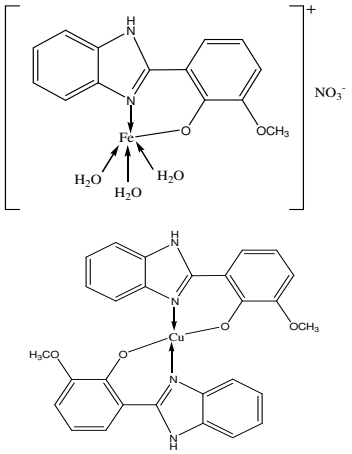


Figure - 26.

2-Methoxy-6-(5-H/methyl/chloro/nitro-1*H*-benzimidazol-2-yl) phenols ligand and its complexes with Fe(II), Cu(II), Ag(I) were synthesized (Figure 27). The antibacterial activity and *MIC* of the free ligands, and the complexes were evaluated using disk diffusion method, and dilution method, respectively, against bacteria. Ligand as well as the Cu(II) and Zn(II) complexes, showed antibacterial activity against gram positive bacteria [61].



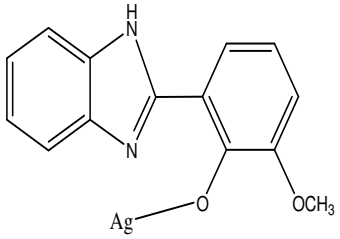


Figure - 27.

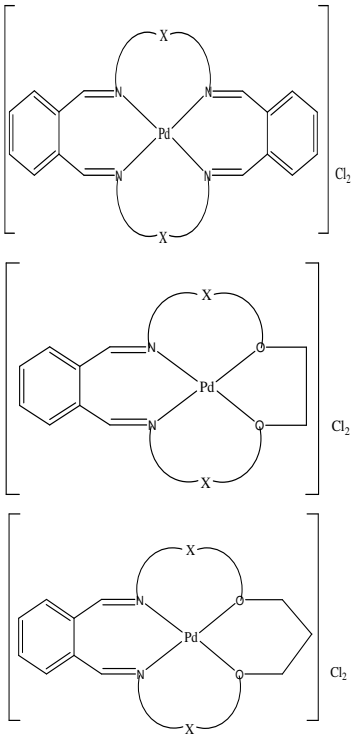


Figure - 28.

New macrocyclic Schiff base Pd(II) compounds were synthesized (Figure 28). The biological activities of all the macrocycles and macrocyclic Pd(II) compounds have been tested against gram positive *Bacillus subtilis,* and *Staphylococcus aureus* and gram negative *Escherichia coli,* and *Klebsiella pneumonia* bacteria and found to be more active than commercially available antibacterial drugs [62].

A novel macrocyclic Cr(III) compounds have been synthesized by treating tetraaza macrocycle ligand (Figure 29). The biological activities of these complexes have been tested in vitro to evaluate their activity against gram positive and gram negative bacteria and were found to be more active than drugs [63].

A new series of complexes have been synthesized by template condensation of oxalyldihydrazide and benzil in the presence of metal salts forming complexes of the type $[M(C_{32}H_{24}N_8O_4)X]X_2$ where M = Cr(III), Mn(III), and Fe(III) and X = Cl^-, NO_3^-, OAc^- (Figure 30). The biological activities of the metal complexes have been tested in vitro against a number of pathogenic bacteria to assess their inhibiting potential. Some of these complexes have been found to exhibit remarkable antibacterial activities [64].

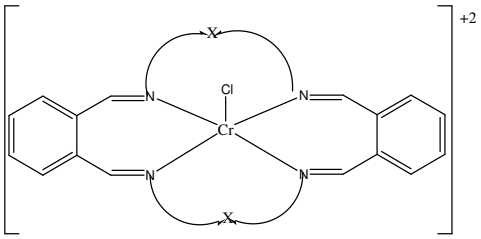


Figure - 29.

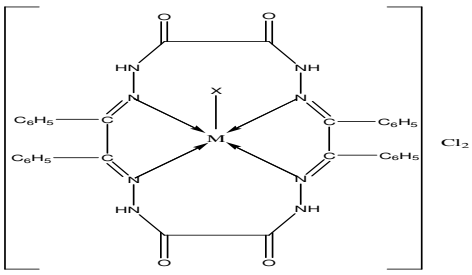


Figure - 30.

Synthesis, and biological studies of some Mn(III) complexes of tetraaza Schiff base macrocycles are described. The ligands were obtained by condensation of O-phthalaldehyde with diamine (Figure 31). These complexes were also tested for their *in vitro* antimicrobial activities against some bacterial strains to assess their inhibiting potential and the activities shown by these complexes were compared with standard drugs [65].

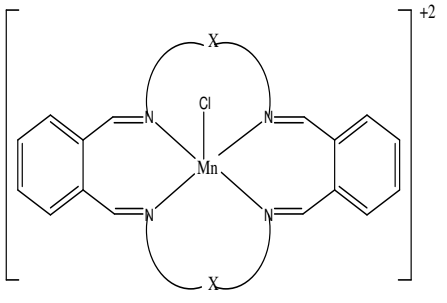


Figure - 31.

Co(II), Ni(II), Cu(II) and Zn(II) complexes of the Schiff base derived from vanillin and dl-aminobutyric acid were synthesized (Figure 32). Antibacterial results indicated that the metal complexes are more active than the ligand [66].

The Schiff base ligands (a) and (b) were prepared. The Cr(III), Co(II), Ni(II), and Ag(I) complexes of the ligands (a) and (b) were prepared (Figure 33). The free ligands and their metal complexes were screened for their antimicrobial activities. The results indicated that the ligands do not have any activity, whereas their

complexes showed more activity against the same organisms [67].

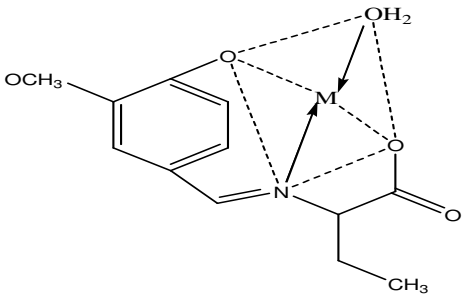


Figure - 32.

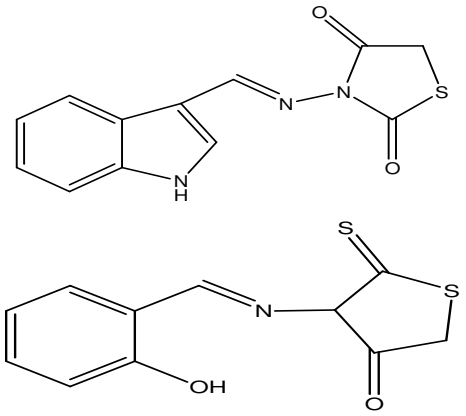


Figure - 33.

A series of metal(II) unsymmetrical Schiff-base complexes, where M = Ni(II), Cu(II), and Zn(II), and their 2,20-dipyridine(bipy) and 1,10-phenanthroline(phen) adducts were synthesized (Figure 34). The antimicrobial activity of the compounds against ten bacteria is reported. The Cu(II) and Zn(II) complexes showed good activity against many of the organisms while their adducts are generally not sensitive [68].

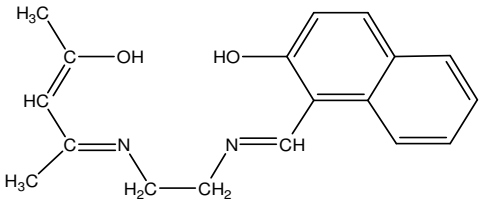


Figure - 34.

Ru(II) complexes of the Schiff bases derived from 3-hydroxyquinoxaline 2-carboxaldehyde and o-phenylenediamine, o-aminophenol or 2-aminobenzimidazole have been prepared (Figure 35). The synthesized ligands and complexes have been tested for in vitro growth inhibitory activity against gram positive and gram negative bacteria[69].

Complexes of the type $[Ru(CO)(EPh_3)(B)(L)]$ (E = P or As, B = PPh_3, $AsPh_3$, py L = dianion of the Schiff bases derived from thiosemicarbazone with acetoacetanilide, acetoacet-*o*-toluidide and *o*-chloro acetoacetanilide) have been synthesized from the reactions of equimolar amounts of $[RuHCl(CO)(EPh_3)_2(B)]$ and Schiff bases (Figure 36). The complexes also exhibited antibacterial activity against different bacteria. The activity was compared with standard drug [70].

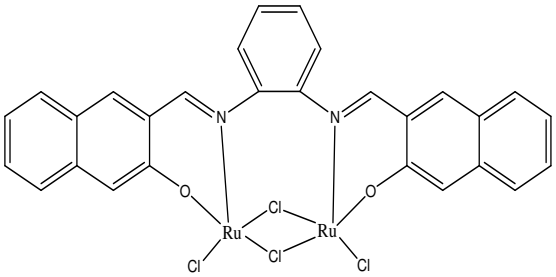


Figure - 35.

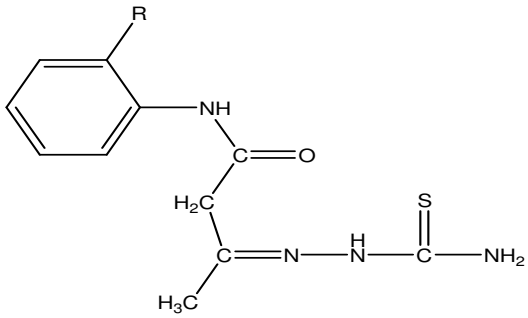


Figure - 36.

A series of new azomethine derivatives were synthesized by reacting 2-formylphenoxyacetic acid with aromatic amines (Figure 37). The compounds were assayed by the disc diffusion method for antibacterial activity against different bacteria. The compounds tested, exhibited good antibacterial activity, almost equal to used standard [71].

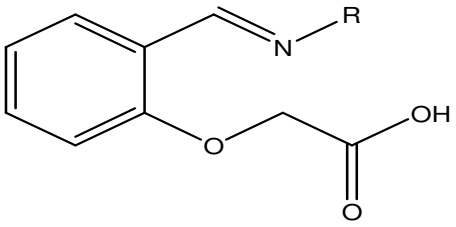


Figure - 37.

A novel series of complexes of the type $[M(TML)X_2]$, where TML is a tetradentate macrocyclic ligand M = Co(II), Ni(II), Cu(II), and Zn(II), X = Cl^-, OAc^-, and NO_3^- have been synthesized by template condensation of benzil and thiocarbohydrazide in the presence of divalent metal salts (Figure 38). The biological activities of metal complexes have been tested in vitro against a number of pathogenic bacteria to assess their inhibiting potential [72].

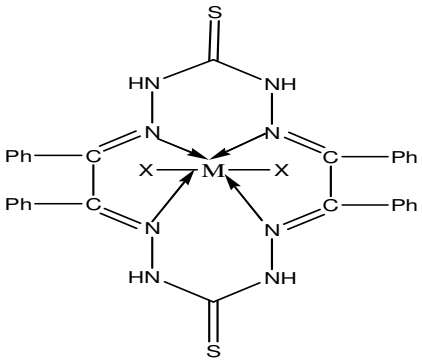


Figure - 38.

Stable Ru(II) carbonyl complexes having the general composition [RuCl(CO)(PPh_3)(B)(L)] (where B = PPh_3, pyridine, piperidine or morpholine, L= anion of bidentate Schiff bases were synthesized from the reaction of [RuHCl(CO)(PPh_3)$_2$(B)] with bidentate Schiff base ligands derived from condensation of *o*-vanillin with primary amines such as methylamine, 2-aminopyridine and cyclohexylamine (Figure 39). The Schiff bases and their Ru(II) complexes have been tested in vitro to evaluate their activity against bacteria [73].

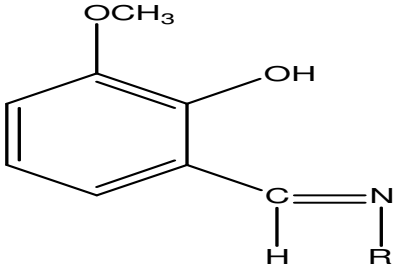


Figure - 39.

Neutral complexes of Cu(II) have been synthesised from the Schiff bases derived from salicylidene-4-aminoantipyrine and $PhNH_2$/substituted anilines (Figure 40). The antimicrobial activity of the ligands and their copper complexes against the bacteria are also reported. The complexes have higher activities than those of the free Schiff bases. Moreover, they have higher activity than control except for *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*[74].

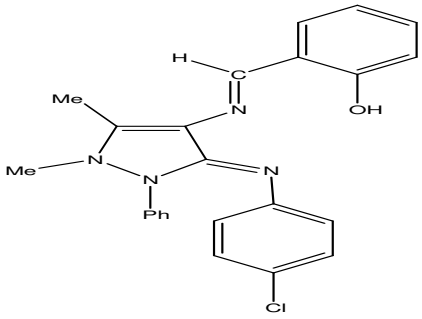


Figure - 40.

A new series of coordination compounds of the starting materials [Cu(dienX_2Y_2)] and their adducts [Cu(dienXXY_2)(2a-5mt)] (where dien = diethylenetriamine, dienXX = Schiff bases of diethylenetriamine with 2-furaldehyde or 2-thiophene-carboxaldehyde, X = O, S, Y = Cl^-, Br^-, and NO_3^-) were synthesized (Figure 41). The study of the biological activity of the compounds against of bacteria showed that the adducts of the type [Cu(dienXXY_2)(2a-5mt)] exhibit increased activity in bacteria, compared to the starting material of type [Cu(dienXXY_2)][75].

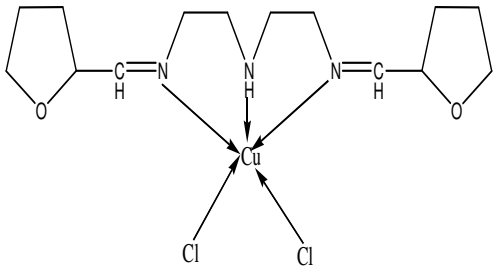


Figure - 41.

Macrocyclic ligands have been prepared by the reaction of the precursor diketone (benzil, glyoxal, diacetyl or 2,3-pentanedione) with a diamine (thiosemicarbazide or semicarbazide). Cu(II) complexes of these ligands have been synthesized (Figure 42). The macrocyclic complexes show more antibacterial activity as compared to the ligands. The antibacterial activities of the compounds were tested against pathogenic bacterial strain[76].

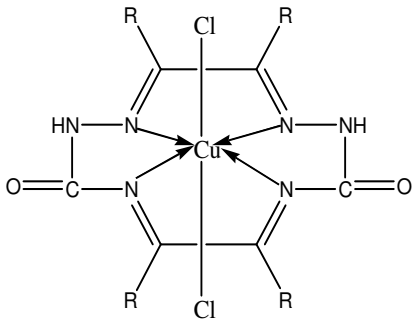


Figure - 42.

3. ANTIFUNGAL ACTIVITY

Fungal infections are not usually limited to the superficial tissues; indeed, a significant increase in life threatening systemic fungal infections has been reported. The fundamental reason for this is the increasing number of patients at risk, including those with advanced age, major surgery, immunosuppressive therapy, acquired immunodeficiency syndrome (AIDS), cancer treatment, and solid-organ and hematopoietic stem cell transplantation. The search and development of more effective antifungal agents are mandatory and some Schiff

bases are known to be promising antifungal agents.

New Co(II) and Ni(II) complexes of 4N-substituted thiosemicarbazones derivatives of 2-methylcyclohexanone (Figure 43) of general composition ML_2X_2 where M = Co(II), and Ni(II), X = Cl^-, SCN^-, and SO_4^{-2} have been prepared. 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 [77].

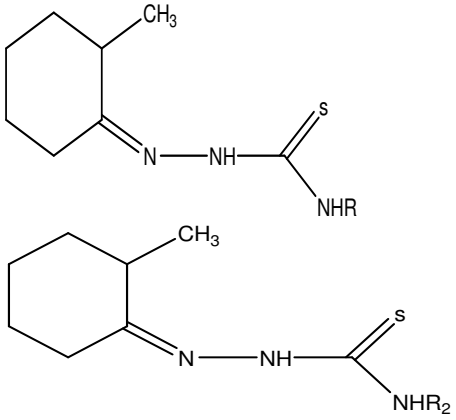


Figure - 43.

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 (Figure 44). In vitro the ligand and its complexes were tested against two pathogenic fungi to assess their growth inhibiting potential [78].

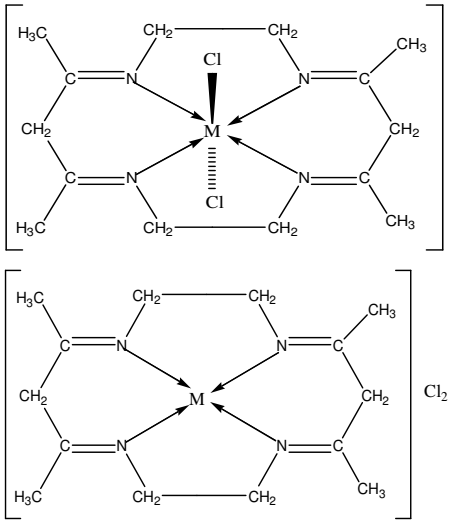


Figure - 44.

Metal complexes (M = Co(II) and Cu(II) and X = Cl^-) of a novel 18-membered macrocyclic ligand (3,4,12,13-tetraphenyl-1,2,5,6,10,11,14,15-octaazacyclooctadecane-7,9,16,18-tetraone 2,4,11,13-tetraene) have been synthesized (Figure 45). All the complexes have been screened for their in vitro antifungal activity. The compounds exhibit significant antifungal activity [79].

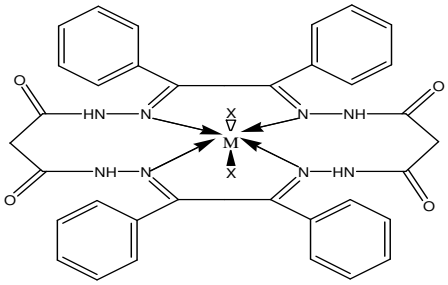


Figure - 45.

A novel series of complexes of the type $[M(C_{28}H_{24}N_4)X]X_2$, where M = Cr(III), Fe(III), and Mn(III), X = Cl^-, NO_3^-, OAc^- and ($C_{28}H_{24}N_4$) 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 (Figure 46). 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 [80].

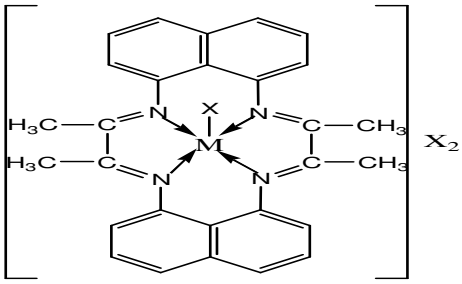


Figure - 46.

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^-, NO_3^- and NCS^- (Figure 47). 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 [81].

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 (Figure 48). The ligand and its complexes were screened for fungicidal activity against two pathogenic fungi to assess their growth inhibiting potential [82].

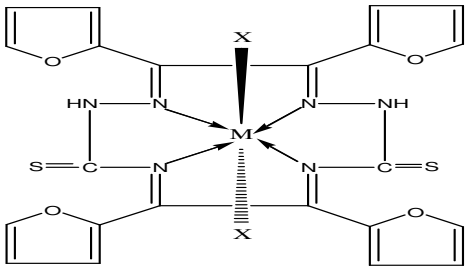


Figure - 47.

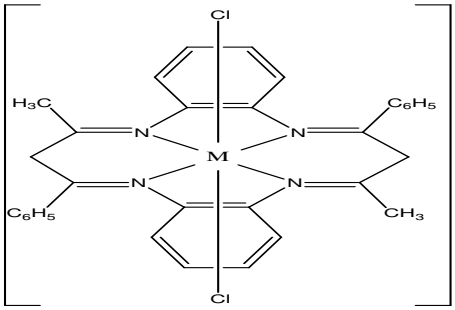


Figure - 48

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 $[MLX_2]$ 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^-, NO_3^-, NCS (Figure 49). The antifungal activities of complexes have been studied against a number of pathogenic fungi. The complexes showed good antifungal results [83].

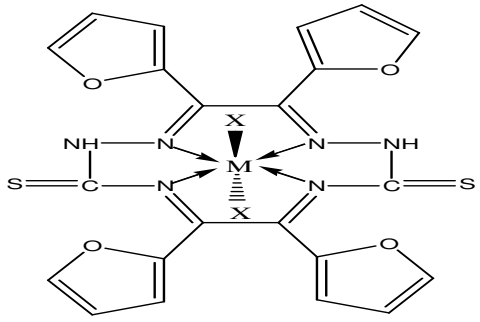


Figure - 49.

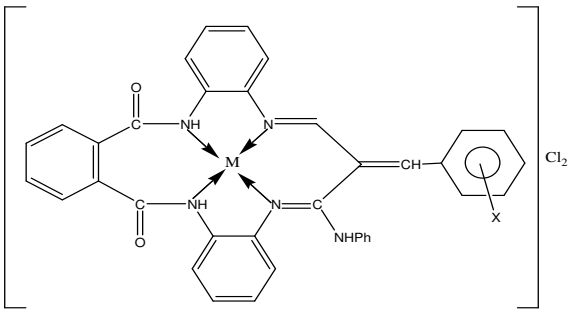


Figure - 50.

The macrocyclic ligands have been synthesized by the condensation reaction of diethyl phthalate with Schiff bases derived from o-phenylenediamine and Knoevenagel condensed β-ketoanilides (Figure 50). The antifungal activities of the compounds were tested against fungi. All complexes showed stronger antifungal activities than free ligands [84].

4. CONCLUSION

These Schiff base ligands and their metal complexes have been investigated as potential antimicrobial agents in long history of medical application. Up to now, a great variety of these ligands and their complexes containing hetero atoms represent good antimicrobial activity. However, the biological activity of these Schiff base ligands and their metal complexes deserves further investigation for better result in research field. Although the research on this subject is incipient, a number of reports disclosing the effects of the Schiff bases on the pathogens of clinical interest have recently been increasing. Schiff base compounds have been shown to be promising leads for the design of more efficient biologically active metal complexes.

Acknowledgement

We greatly acknowledge to the Central Science Library (CSL), University of Delhi, as well as to the principal of Zakir Husain Delhi College, University of Delhi UGC and DRDO Delhi for providing facility for this work.

5. REFRENCES

1. Chandra S and Sharma SD. Chromium(III), manganese(II), cobalt(II), nickel(II), copper(II) and palladium(II) complexes of a 12-membered tetraaza $[N_4]$ macrocyclic ligand. **Trans. Met. Chem.,** 2002; 27:732-739.
2. Chandra S and Kumar R. Synthesis and spectroscopic characterization of transition metal complexes of a 12-membered tetraaza $[N_4]$ macrocyclic ligand and their biological activity. **Trans. Met. Chem.,** 2004; 29:2693-2704.
3. Malachowski MR, Dorsey BT, Parker MJ, Adams ME and Kelly RS. Synthesis, characterization, and X-ray crystal structure of cobalt(III) complexes with a N_2O_2-donor Schiff base and ancillary ligands: Spectral, antibacterial activity, and electrochemical studies. **Polyhedron.,** 1998; 17:1289-1296.
4. Arulmurugan S, Kavitha HP and Venkatraman BR. Biological activities of Schiff base and its complexes: a review. **Rasayan J. Chem.,** 2010; 3(3):385-410.
5. Kumar D, Chadda S, Sharma J and Surain P. Syntheses, Spectral characterization, and

antimicrobial studies on the coordination compounds of metal ions with schiff base containing both aliphatic and aromatic hydrazide moieties. **Bioinorg. Chem. Appl.,** (http://dx.doi.org/10.1155/2013/981764).

6. Maclachlan MJ, Park MK and Thompson LK. Coordination compounds of schiff-base ligands derived from diaminomaleonitrile (DMN): mononuclear, dinuclear, and macrocyclic derivatives. **Inorg. Chem.,** 1996; 35(19): 5492-5499.
7. Malik S, Ghosh S and Mitu L. Complexes of some 3d-metals with a schiff base derived from 5-acetamido-1,3,4-thiadiazole-2-sulphonamide and their biological activity. **J. Serb. Chem. Soc.,** 2011; 76(10): 1387-1394.
8. Phaniband MA and Dhumwad SD. Synthesis, characterization and biological studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes of schiff bases derived from 4-substituted carbostyrils[quinolin2(1H)-ones]. **Trans. Met. Chem.,** 2007; 32(8): 1117-1125.
9. Chandra S, Jain D, Sharma AK and Sharma P. Coordination modes of a schiff base pentadentate derivative of 4-aminoantipyrine with cobalt(II), nickel(II) and copper(II) metal ions: synthesis, spectroscopic and antimicrobial studies. **Molecules.,** 2009; 14(1): 174-190.
10. Naeimi H, Safari J and Heidarnezhad A. Synthesis of schiff base ligands derived from condensation of salicylaldehyde derivatives and synthetic diamine. **Dyes and Pigments.,** 2007; 73(2):251-253.
11. Sharma AK and Chandra S. Synthesis, structural and fungicidal studies of hydrazone based coordination compounds. **Spectrochim. Acta Part A.,** 2013; 103(15): 96-100.
12. Tyagi M, Chandra S, Akhtar J and Chand D. Modern spectroscopic technique in the characterization of biosensitive macrocyclic Schiff base ligand and its complexes: Inhibitory activity against plant pathogenic fungi. **Spectrochimica Acta Part A.,** 2014; 118(24): 1056-1061.
13. Chandra S and Agrawal S. Spectroscopic characterization of lanthanoid derived from a hexadentate macrocyclic ligand: Study on antifungal capacity of complexes. **Spectrochimica Acta Part A.,** 2014; 124(24): 564-570.
14. Neelakantan MA, Esakkiimmal M, Mariappan SS, Dharmaraja J and Jeyakumar T. Synthesis characterization and biological activities of some schiff-base metal complexes. **Ind. J. Pharma. Sci.,** 2010; 72(2): 216-222.
15. Fugu MB, Ndahi NP, Paul BB and Mustapha AN. Synthesis, characterization, and antimicrobial studies of some vanillin schiff base metal (II) complexes. **J. Chem. Pharma. Res.,** 2013; 5(4):22-28.
16. Patil AR, Donde KJ, Raut SS, Patil VR and Lokhande RS. Synthesis, characterization and biological activity of mixed ligand Co(II) complexes of schiff base 2-amino-4-nitrophenol-n-salicylidene with some amino acids. **J. Chem. Pharma. Res.,** 2012; 4(2):1413-1425.
17. Prakash A and Adhikari D. Application of Schiff bases and their metal complexes-a review. **Int. J. Chem Tech Res.,** 2011; 3(4):1891-1896.
18. Sirajuddin M, Uddin N, Ali S and Tahir MN. Potential bioactive schiff base compounds: synthesis, characterization, X-ray structures, biological screenings and interaction with salmon sperm DNA. **Spectrochim. Acta Part A.,** 2013; 116:111-121.
19. Abdel-Wahed MG, Refat MS and El-Megharbel SM. Spectroscopic, thermal and biological studies of coordination compounds of sulfasalazine drug: Mn(II), Hg(II), Cr(III), ZrO(II), VO(II) and Y(III) transition metal complexes. **Bull. Mater. Sci.,** 2009; 32(2): 205-214.
20. Ispir E, Toroglu S and Kayraldiz A. Synthesis and antimicrobial activity of new schiff bases having the –SiOR group (R = CH_3 *or* CH_2CH_3), and their transition metal complexes. **Trans. Met. Chem.,** 2008; 33:953-960.
21. Tarafder MTH, Ali MA, Wee DJ, Azahari K, Silong S and Crouse KA. Complexes of a tridentate ONS schiff base. synthesis and biological properties. **Trans. Met. Chem.,** 2000; 25: 456-460.
22. Chohan ZH, Munawar A and Supuran C. Transition metal ion complexes of schiff-bases. synthesis, characterization and antibacterial properties. **Met Based Drugs.** 2001; 8(3): 137-143.
23. Schwartz JA, Lium EK and Silverstein SJ. Herpes simplex virus type 1 entry is inhibited by the cobalt chelate complex CTC-96. **J. Virol.,** 2001; 75: 4117-4128.
24. Halliwell B and Gutteridge JM. Role of free radicals and catalytic metal ions in human disease: an overview. **Methods Enzymol.,** 1990; 186:1-85.

25. Puszko A, Wasylina L, Pelczynska M, Staszak Z, Adach A, Cieslak-Golonka M and Kubiak M. Methyl-substituted 4-nitropyridine N-oxides as ligands: structural, spectroscopic, magnetic and cytotoxic characteristics of copper(II) complexes. **J. Inorg. Biochem.,** 2007; 101(1):117-126.
26. Zhou CY, Zhao J, Wu YB, Yin CX and Pin Y. Synthesis, characterization and studies on DNA-binding of a new Cu(II) complex with N_1,N_8-bis(1-methyl-4-nitropyrrol-2-ylcarbonyl)triethylenetetramine. **J. Inorg. Biochem.,** 2007; 101(1):10-18.
27. Ahmed RM, Yousif EI, Hasan HA and Al-Jeboori MJ. Metal complexes of macrocyclic schiff-base ligand: preparation, characterisation, and biological activity. (http://dx.doi.org/10.1155/2013/289805).
28. Omar MM and Ibrahim AA. Biological activity studies on metal complexes of novel tridentate schiff base ligand. **Spectroscopic and thermal characterization.** 2009; 44(12): 4801-4812.
29. Singh DP, Kumar K and Sharma C. New 14-membered octaaza macrocyclic complexes: Synthesis, spectral, antibacterial and antifungal studies. 2010; 45(3):1230-1236.
30. Patil SA, Kumar U, Kamble V and Badami PS. Biologically active 22-membered N4 tetraaza macrocyclic triazoles: Template synthesis and spectroscopic approach. **Der Pharma Chemica.,** 2009; 1(2): 210-227.
31. Spinu C, Pleniceanu M and Tigae C. Biologically active transition metal chelates with a 2-thiophenecarboxaldehyde-derived schiff base: synthesis, characterization, and antibacterial properties. **Turk. J. Chem.,** 2008; 32:487-493.
32. Baluja S, Solanki A and Kachhadia N. Evaluation of biological activities of some schiff bases and metal complexes. **J. Iran. Chem. Soc.,** 2006; 3:312-317.
33. Fugu MB, Ndahi NP, Paul BB and Mustapha AN. Synthesis, characterization, and antimicrobial studies of some vanillin schiff base metal (II) complexes. **J. Chem. Pharma. Res.,** 2013; 5(4): 22-28.
34. Tyagi M and Chandra S. Synthesis and spectroscopic studies of biologically active tetraazamacrocyclic complexes of Mn(II), Co(II), Ni(II), Pd(II) and Pt(II). **Saudi Chem. Soc.,** 2014; 18(1):53-58.
35. Sari N, Arslan S, Logoglu E and Sakiyan. Spectroscopic and biological activity studies on tridentate Schiff base ligands and their transition metal complexes. **Ind. J. Sci.,** 2003; 16:283-288.
36. Usharani M, Akila E and Rajavel R. Synthesis and spectral investigations of binuclear schiff base metal complexes derived from 1,5-diaminonaphthalene. **J. Chem. Bio. Phy. Sci.,** 2012; 2:677-682.
37. Rai BK, Kumari R and Thakur A. Antimicrobial screening of Co(II), Ni(II) and Cu(II) Complexes with nitrogen and oxygen containing schiff base. **Ori. J. Chem.,** 2012; 28: 943-948.
38. Sunitha M, Jogi P, Ushaiah and Gyanakumari C. Synthesis, structural characterization, molecular modelling and antimicrobial studies of transition metal complexes of schiff base ligand derived from 5-chlorosalicylaldehyde and 2-(2-aminophenyl) 1*H*-benzimidazole. **J. Chem. Pharma. Res.,** 2012; 4(3):1553-1561.
39. Reddy PM, Rohini R, Krishna ER, Hu A and Ravinder V. Synthesis, spectral and antibacterial studies of copper(II) tetraaza macrocyclic complexes. **Int. J. Mol. Sci.,** 2012; 13:4982-4992.
40. Ahmadi RA and Amani S. Synthesis, spectroscopy, thermal analysis, magnetic properties and biological activity studies of Co(II) and Co(II) complexes with schiff base dye ligands. **Molecules,** 2012; 17:6434-6448.
41. Singh DP, Grover V, Kumar K and Jain K. Synthesis and characterization of divalent metal complexes of the macrocyclic ligand derived from isatin and 1,2-diaminobenzene. **J. Serb. Chem. Soc.,** 2011; 76(0):1-9.
42. Budige G, Puchakayala MR, Kongara SR, Hu A and Vadde R. Synthesis, characterization and biological evaluation of mononuclear Co(II), Ni(II), Cu(II) and Pd(II) complexes with new N_2O_2 schiff base ligands. **Chem. Pharm Bull,** 2011; 59(2):166-171.
43. Al-Amiery AA, Al-Majedy YK, Abdulreazak H and Abood H. Synthesis, characterization, theoretical crystal structure, and antibacterial activities of some transition metal complexes of the thiosemicarbazone (Z)-2-(pyrrolidin-2-ylidene)hydrazinecarbothioamide. **Bioinorg Chem. Appl.,** (doi:10.1155/2011/483101).
44. Anuradha K and Rajavel R. Synthesis, spectral characterization and biological activity of new symmetrical macrocyclic binuclear schiff base complexes. **Int. J. Pharma. Tech.,** 2011; 3:2217-2227.
45. Prakash A, Gangwar MP and Singh KK. Synthesis, spectroscopy and biological studies

of nickel (II) complexes with tetradentate schiff bases having N_2O_2 donor group. **J. Develop. Bio. Tissue Eng.,** 2011; 3(2):13-19.

46. Mohamed GG, Omar MM, El-Ela MSA and Hindy AMM. Preparation of macrocyclic Schiff-base ligand and antibacterial activities of transition metal complexes thereof. **Toxicol. Enviro. Chem.,** 2011; 93:57-72.
47. Sharma R, Prabhat, Singh R, Pawar S and Chauhan A. Studies of transition metal complexes and their antibacterial activities. **J. Am. Sci.,** 2010; 6(9):559-564.
48. Olar R, Badea M, Marinescu D, Chifiriuc MC, Bleotu C, Grecu MN, Iorgulescu EE and Lazar V. N,N-dimethylbiguanide complexes displaying low cytotoxicity as potential large spectrum antimicrobial agents. **Eur. J. Med. Chem.,** 2010; 45:3027-3034.
49. Khanmohammadi H, Amani S, Abnosi MH and Khavasi HR. New asymmetric heptaaza schiff base macrocyclic complex of Mn(II): crystal structure, biological and DFT studies. **Spectrochim Acta PartA.,** 2010; 77: 342-347.
50. Sellappan R, Prasad S, Jayaseelan P and Rajavel R. Synthesis, spectral characterization, electrochemical and antimicrobial activity of macrocyclic Schiff base vanadyl complexes. **Rasayan J Chem.,** 2010; 3:556-562.
51. Pawar V, joshi S and Uma V. Synthesis, characterization and biological evaluation of macrocyclic schiff bases with oxovanadium (V) complexes. **Der Pharma Chemica,** 2010; 2(5):377-382.
52. Singh DP and Kumar K. Synthesis, spectroscopic studies, and antibacterial activities of 14-membered tetraazamacrocyclic complexes of divalent transition metal ions. **J. Coord. Chem.,** 2010; 63: 4007-4016.
53. Saadeh SM. Synthesis, characterization and biological properties of Co(II), Ni(II), Cu(II) and Zn(II) complexes with an SNO functionalized ligand. **Arab. J. Chem.,** 2010; 6:191-196.
54. Singh DP, Malik V, Kumar R and Kumar K. Synthesis and spectral study of biologically active macrocyclic complexes of divalent transition metal ions. **Rus. J. Coord. Chem.,** 2010; 36:220-225.
55. Singh DP, Grover V, Kumar K and Jain K. Metal on prompted macrocyclic complexes derived from Indole-2,3-dione (isatin) and *o*-phenylenediamine with their spectroscopic and antibacterial studies. **Acta Chim. Slov.,** 201; 57:775-780.
56. Mohamed GG, Omar MM and Ibrahim AA. Preparation, characterization and biological activity of novel metal-NNNN donor schiff base complexes. **Spectrochim Acta Part A** 2010; 75: 678-685.
57. Singh BK, Prakash A, Rajour HK, Bhojak N and Adhikari D. Spectroscopic characterization and biological activity of Zn(II), Cd(II), Sn(II) and Pb(II) complexes with schiff base derived from pyrrole-2 carboxaldehyde and 2-amino phenol. **Spectrochim Acta Part A** 2010; 76: 376-383.
58. Singh DP, Kumar K, Kumar R and Singh J. Template synthesis and characterization of biologically active transition metal complexes comprising 14-membered tetraaza macrocyclic ligand. **J. Serb. Chem. Soc.** 2010; 75(2):217-228.
59. Rao YS, Prathima B, Reddy SA, Madhavic K and Reddy AV. Complexes of Cu(II) and Ni(II) with Bis(phenylthiosemicarbazone): synthesis, spectral, epr and *in vitro*-antibacterial and antioxidant activity. **J. Chin. Chem. Soc.,** 2010; 57:677-682.
60. Badwaik VB, Deshmukh RD and Aswar AS. Transition metal complexes of a schiff base: synthesis, characterization, and antibacterial studies. **J. Coord. Chem.,** 2009; 62:2037-2047.
61. Tavman A, Ikiz S, Bagcigil AF and Ozgur NY. Preparation, characterization and antibacterial effect of 2-methoxy-6-(5-H/Me/Cl/NO2-1*H*-benzimidazol-2-yl)phenols and some transition metal complexes. **J. Serb. Chem. Soc.** 2009; 74(5): 537-548.
62. Shanker K, Reddy PM, Rohini R, Ho Y-P and Ravinder V. Encapsulation of Pd(II) by N_4 and N_2O_2 macrocyclic ligands: their use in catalysis and biology. **J. Coord. Chem.,** 2009; 62: 3040-3049.
63. Reddy PM, Shanker K, Rohini R and Ravinder V. Antibacterial active tetraaza macrocyclic complexes of chromium (III) with their spectroscopic approach. **Int. J. Chem. Tech Res.,** 2009; 1: 367-372.
64. Singh DP, Kumar R and Singh J. Synthesis and spectroscopic studies of biologically active compounds derived from oxalyldihydrazide and benzil, and their Cr(III), Fe(III) and Mn(III) complexes. **Eur. J. Med. Chem.,** 2009; 44:1731-1736.
65. Shanker K, Ashok M, Reddy PM, Rohini R and Ravinder V. Spectroscopic characterization and antibacterial activities of Mn(III) complexes containing the tetradentate aza

schiff base ligands. **Int. J. Chem Tech Res.,** 2009; 1:777-783.

66. Nair MS and Joseyphus RS. Synthesis and characterization of Co(II), Ni(II), Cu(II) and Zn(II) complexes of tridentate schiff base derived from vanillin and DL-aminobutyric acid. **Spectrochim Acta Part A.,** 2008; 70: 749-753.
67. Elzahany EA, Hegab KH, Khalil SKH and Youssef NS. Synthesis, characterization and biological activity of some transition metal complexes with schiff bases derived from 2-formylindole, salicyladehyde, and n-amino rhodanine. **Aus. J. Basic Applied Sci.,** 2008; 2(2): 210-220.
68. Osowole AA, Kolawole GA and Fagade OE. Synthesis, characterization and biological studies on unsymmetrical Schiff-base complexes of nickel(II), copper(II) and zinc(II) and adducts with 2,20-dipyridine and 1,10-phenanthroline. **J. Coord. Chem.,** 2008; 61:1046-1055.
69. Chittilappilly S and Yusuff KKM. Synthesis charaecterization and biological properties derived from 3-hydroxyquinoxaline-2-carboxaldehyde and salicylaldehyde. **Ind. J. Chem.,** 2008; 47A: 848-853.
70. Musa MA, Khan MO, Aspedon A and Cooper wood JS. Synthesis and antimicrobial activity of N,N'-bis(2-hydroxylbenzyl)-1,2-ethanediamine derivatives. **Lett. Drug. Des. Discov.,** 2010; 7(3): 165-170.
71. Iqbal A, Siddiqui HL, Ashraf CM, Ahmad M and Weaver GW. Synthesis, characterization and antibacterial activity of azomethine derivatives derived from 2-formylphenoxyacetic acid. **Molecules,** 2007; 12: 245-254.
72. Singh DP and Kumar R. Template synthesis, spectroscopic studies and biological screening of macrocyclic complexes derived from thiocarbohydrazide and benzyl. **Trans. Met. Chem.,** 2006; 31:970-973.
73. Kumar KN and Ramesh R. Synthesis, characterization, redox property and biological activity of Ru(II) carbonyl complexes containing O,N-donor ligands and heterocyclic bases. **Spectrochim. Acta Part A,** 2004; 60: 2913-2918.
74. Raman N, Kulandaisamy A, Thangaraja C, Manisankar P, Viswanathan S and Vedhi C. Synthesis, structural characterisation and electrochemical and antibacterial studies of schiff base copper complexes. **Trans. Met. Chem.,** 2004; 29: 129-135.
75. Chaviara AT, Cox PJ, Repana KH, Papi RM, Papazisis KT, Zambouli D, Kortsaris AH, Kyriakidis DA and Bolos CA. Copper(II) schiff base coordination compounds of dien with heterocyclic aldehydes and 2-amino-5-methyl-thiazole: synthesis, characterization, antiproliferative and antibacterial studies. crystal structure of $CudienOOCl_2$. **J. Inorg. Biochem.,** 2004; 98: 1271-1283.
76. Chandra S, Sangeetika and Thakur S. Electronic, e.p.r., cyclic voltammetric and biological activities of copper(II) complexes with macrocyclic ligands. **Trans. Met. Chem.,** 2004; 29: 925-935.
77. Kumar U and Chandra S. Synthesis, spectroscopic characterization of some schiff base complexes derived from 2-methylcyclohexanone and their activity against some fungi. **J Saudi Chem. Soc.,** 2011; 15: 19-24.
78. Tyagi M, Chandra S and Choudhary SK. Tetraaza macrocyclic complexes: synthesis, spectral and antifungal studies. **J. Chem. Pharm. Res.,** 2011; 3(1):56-63.
79. Kumar U and Chandra S. Synthesis, spectral and antifungal studies of some coordination compounds of cobalt(II) and copper(II) of a novel 18-membered octaaza $[N_8]$ tetradentate macrocyclic ligand. **J. Saudi Chem. Soc.,** 2011; 15: 187-193.
80. Singh DP and Kumar K. Macrocyclic complexes: synthesis and characterization. **J. Serb. Chem. Soc.,** 2010; 75(4): 475-482.
81. Kumar U and Chandra S. Synthesis, characterization and in vitro antifungal screening of manganese(II) and copper(II) complexes of hexaaza $[N_6]$ macrocyclic ligand. **J. Nepal Chem. Soc.,** 2010; 25: 46-52.
82. Chandra S, Tyagi M and Agarawal S. Synthesis and characterization of a tetraaza macrocyclic ligand and its cobalt(II), nickel(II) and copper(II) complexes. **J. Serb. Chem. Soc.,** 2010; 75(7): 935-941.
83. Kumar U and Chandra S. Biological active cobalt(II) and nickel(II) complexes of 12-membered hexaaza $[N_6]$ macrocyclic ligand synthetic and spectroscopic aspects. **E-J. Chem.,** 2010; 7(4): 1238-1245.
84. Raman N, Joseph J, Kumar AS and Pothiraj C. Antifungal activities of biorelevant complexes of copper(II) with biosensitive macrocyclic ligands. **Mycobio.,** 2006; 34(4):214-218.