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A SHORT REVIEW ON BIOLOGICAL ACTIVITY OF TRIAZOLE CONTAINING METAL COMPLEXES

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ABSTRACT

Triazole ligands and their metal complexes are very important in medicinal and pharmaceutical fields because of their wide spectrum of biological activities. This review describes biological activity on triazole containing metal complexes. Triazoles are regarded as a promising class of bioactive heterocyclic compounds that exhibit a range of biological activities like anti-microbial, anti-viral, anti-diabetic, anti-cancer activity, anti-oxidant, anti-proliferative, anti-HIV, anti-convulsant, anti-inflammatory, etc. These promising results are encouraging further for inorganic as well as bio-inorganic chemists.

KEY WORDS

Triazoles, Schiff bases, Metal complexes and Biological activity.

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INTRODUCTION

Triazole compounds are extensively used in clinic, and are currently one of the most important fields in the researches and developments of drugs. More and more triazole compounds, with strong pharmacological activity, low toxicity, less adverse effects, fewer multi-drug resistances, high bioavailability, good pharmacokinetics property, drug-targeting, diversity of drug administration, broad spectrum and better curative effect etc. are frequently employed as candidates or clinical drugs for the therapy of various types of diseases, which have showed their large development value and wide potential as medicinal agents. Combining with authors, researches and referring other works from

literatures in recent 5 years, this work systematically reviewed the new researches and developments of the whole range of triazole compounds as medicinal drugs, including antifungal, antibacterial, anti-tuberculosis, anticancer, antivirus, anti-inflammatory, anti-convulsion and so on. The perspectives of the foreseeable future in the research and development of triazole compounds as medicinal drugs are also presented. Triazole derivatives have been found to possess various pharmacological activities, such as, anti-inflammatory, analgesics, antipyretic and antifungal.

Metal complexes may constitute one such possible class exhibiting biological activities[1-3]. Schiff bases and their structural analogues, as ligating compounds containing acyclic and cyclic imines, are of great importance in modern coordination chemistry[4] as they easily form stable complexes with most transition metal ions[5,6]. The five membered rings containing two or three nitrogen atoms (azoles) are more important, since the imidazole group of histidine acts as a ligand in most of the known hemoproteins. Imidazole derivatives and 1,2,4-triazoles[7] are considered to be of potential interest to coordination chemists because they can be used to link studies on the metal binding properties of nitrogenous bases with information on the proton affinities in the gas phase[8], in aqueous solutions and aprotic solvents[9] and on their H-bonding capacities[10]. The coordination compounds of 1, 2, 4-triazoles are associated with diverse biological activities such as antimicrobial, anticonvulsant, fungicidal, antitumor, antiviral and analgesic activities[11-15]. We highlight the most significant examples of compounds belonging to this class, which exhibit biological activities to have been reported in the literature.

BIOLOGICAL ACTIVITY OF TRIAZOLE

Anti-Microbial Activity

Infectious diseases have been serious and growing threatens to human health during the past few decades. The decrease of sensibility to anti-microbial agents in current use has also been increasing for a great variety of pathogens and the resistance to multiple drugs is more and more prevalent for several microorganisms, especially for Gram-positive bacteria and some intractable fungi. Their inhibitory properties as regard representative fungi have been extensively exploited. The increase in bacterial resistance has attracted considerable interest in the discovery and development of new classes of anti-bacterial agents. The new agents should preferably consist of chemical characteristics that clearly differ from those of existing agents.

The literature survey of the recent studies done on triazole containing metal complexes indicates that they have antimicrobial activities like anti-bacterial and antifungal activities which have been summarized as given below:

Kiran *et. al*., had synthesized Co(II), Ni(II), Cu(II) and Zn(II) complexes of bidentate triazole ligands derived from the condensation of 4-amino-5-mercapto-3-methyl/ethyl-1,2,4-triazole with 5-nitrofurfuraldehyde and tested as antimicrobial agents. The synthesized triazole ligand act as bidentate ligands and coordinated to the metal ions through nitrogen and sulphur of the thiol group. The bonding of ligand to metal ion is confirmed by elemental analyses, spectral studies (UV–Vis, IR, ^{1}H NMR, Fluorescence), TGA, magnetic and conductance measurements. The ligands and their metal complexes had been screened for both Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram negative (*Pseudomonas aeruginosa* and *Escherichia coli*) and antifungal activity (*Aspergillus niger* and *A. flavus*). Compounds, Zn(**L_1**)(OAc). $3H_2O$ and Zn(**L_2**)(OAc). $3H_2O$ were found to exhibit the highest antibacterial activity and Zn(L_2)(OAc).$3H_2O$ was found to showed the good antifungal property. The antimicrobial studies suggested that the Schiff bases were found to be biologically active and their metal complexes showed significantly enhanced antibacterial and antifungal activities against microbial strains in comparison to the free ligands[16].

Mohamed *et. al*., had synthesized Mn(II), Co(II), Ni(II) and Cu(II) complexes of [(1H-1,2,4-triazole-3-ylimino)methyl]naphthalene-2-ol which is derived from 1,2,4-triazole and 2-hydroxy-1-

naphthaldehyde. The bonding of ligand to metal ion is confirmed by elemental, IR, mass spectra, thermal analyses and magnetic data. The spectral data suggested distorted octahedral and tetrahedral geometry for Cu(II) complexes and tetrahedral geometries for Ni(II), Co(II) and Mn(II) complexes which are consistent with the geometry optimization and conformational analysis. Triazole and its metal complexes had been screened for their in vitro antimicrobial activities against Gram positive bacteria (*Staphylococcus aureus*), Gram negative bacteria (*Escherichia coli* and *Pesudomonas aeruginosa*), fungi (*Asperigllusflavus* and *Mucer*) and yeast (*Candida albicans* and *Malassezia furfur*). The Cu(II) complex contain **L_3** showed activity against all the tested organisms (diameters inhibition zone ranged between 14 and 30 mm) except the yeast, M. furfur. The Ni(II) complex contain **L_3** showed the highest activity against *A. Flavus* with inhibition zone diameter (45 mm). It also showed activity against *E. coli* and *A. flavus*. The Co(II) complex contain **L_3** was active against Gram negative, fungi and *C. albicans*, and gave the highest activity[17].

Zahid *et. al*., had synthesized with a new class of triazole Schiff bases derived from the reaction of 3,5-diamino-1,2,4-triazole with 2-hydroxy-1-naphthaldehyde, pyrrole-2-carboxaldehyde, pyridine-2-carboxaldehyde and acetyl pyridine-2-carboxaldehyde, respectively. The synthesized new series of triazole Schiff bases act as bidentate ligands and coordinate with the vanadium(IV) metal through azomethine-N, deprotonated-O and/or deprotonated-N. This binding of the triazole Schiff bases to the vanadium(IV) metal is confirmed by physical (magnetic susceptibility, molar conductance), spectral (IR, ^{1}H NMR, ^{13}C NMR, mass and electronic) and analytical data. The triazole Schiff bases and their oxovanadium(IV) complexes had been studied for *in vitro* antibacterial activity against four Gram-negative (*Escherichia coli*, *Shigella flexenari*, *Pseudomonas aeruginosa*, *Salmonella typhi*) and two Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) bacterial strains, *in vitro* antifungal activity against *Trichophyton longifucus*, *Candida albican*, *Aspergillus flavus*, *Microscopum canis*, *Fusarium solani* and *Candida glaberata*. The antibacterial results of the oxovanadium(IV) complexes contain **L_5** and **L_6** were considered the most active compounds due to the presence of more number of nitrogen atoms. Therefore, the MIC values of these compounds contain **L_5** and **L_6** were found at 1.642 x 10^{-7} and 1.347 x 10^{-6} M, respectively. The antifungal results of compound contain **L_4-L_6** possessed significant (55-81%) activity against all strains. The simple triazole schiff bases showed weaker to significant activity against one or more bacterial and fungal strains. In most of the cases higher activity was exhibited upon coordination with vanadium(IV) metal[18].

Kiran *et. al*., had synthesized new organosilicon(IV) and organotin(IV) complexes by the reaction Me_2MCl_2 (M= Si and Sn) with new ligands, 4-[(4-cyano-benzylidene)-amino]-5-mercapto-1,2,4-triazole and 4-[(4-Cyano-benzylidene)-amino]-5-mercapto -3-methyl-1,2,4-triazole in absolute methanol. The metal complexes had been proposed to have trigonal bipyramidal and octahedral geometries. This geometry was confirmed by the elemental analyses, molar conductance and spectral (UV, FT-IR, ^{1}H, ^{13}C, ^{29}Si and ^{119}Sn NMR) studies. *In vitro* antimicrobial activities of the compounds were evaluated. Me_2Sn **(L_7)**$_2$ was found to possess highest antimicrobial activity[19].

Muhammad Hanif et.al., had synthesized Co(II), Ni(II), Cu(II) and Zn(II) complexes of triazole derived from Schiff base ligands in equimolar reaction of 3-amino-1H-1,2,4-triazole with pyrrol-2-carboxaldehyde, 4-bromo-thiophene-2-carboxaldehyde and 5-iodo-2-hydroxy benzaldehyde. All the newly synthesized Schiff bases ligands act as tridentate ligands and all these are coordinated through the azomethine-N, triazole ring-N and hydroxyl-O to the metal ion. All the synthesized metal (II) complexes possessed an octahedral geometry except the Cu (II) complexes which showed a distorted octahedral geometry. The structure and bonding nature of all the compounds were identified by their physical, spectral and

analytical data. All the synthesized compounds were studied for their *in vitro* antibacterial and antifungal activities against four Gram-negative (*Escherichia coli, Shigella sonnei, Pseudomonas aeruginosa* and *Salmonella typhi*) and two Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) bacterial strains and against six fungal strains (*Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani* and *Candida glabrata*) by using agar-well diffusion method. The bacterial activity data of metal(II) complexes exhibited that the complexes contains $\mathbf{L_8}$, $\mathbf{L_9}$ and $\mathbf{L_{10}}$ showed significant activity (54–82%) against all the tested bacterial strains, while the complexes 4 and 9 showed significant activity (57–83%) and moderate activity (48–52%) against bacterial strains[20].

Singh *et.al*., had synthesized Zn(II) complexes by the reactions of zinc(II) acetate with bidentate ligands of triazole Schiff bases derived from 3-substituted phenyl-4-amino-5-hydrazino-1, 2, 4-triazole and benzaldehyde,2-hydroxyacetophenone or indoline-2,3-dione. They were characterized by Elemental analyses, FT-IR, ^{1}H NMR, ^{13}C NMR and FAB mass. All these triazole Schiff bases and their complexes have also been screened for their antibacterial activities against *Bacillus subtilis, Escherichia coli* and antifungal activities against *Colletotrichum falcatum, Aspergillus niger, Fusarium oxysporium* and *Carvularia pallescence* by petriplates methods. The compound $[Zn\mathbf{L_{11}}(H_2O)_2]$ is more active against all bacteria and fungi because they have additional heterocyclic ring (indoline-2,3-dione) [21].

Bagihalli *et. al*., had synthesized a series of metal complexes of Zn(II) with newly synthesized 1,2,4-triazole Schiff bases derived from the condensation of 3-substituted-4-amino-5-mercapto-1,2,4-triazole with 8-formyl-7-hydroxy-4-methylcoumarin. The structure of the complexes has been proposed in the light of elemental analyses, spectroscopic data (IR, UV-Vis, ^{1}H NMR and FAB-mass), thermal studies. All these Schiff bases and their complexes have also been screened for their antibacterial (*Escherichia. coli, S. aureus, S. pyogenes, P. aeruginosa* and *Salmonella typhi*) and antifungal activities (*Aspergillus niger, Aspergillus flavus* and *cladosporium*) by MIC method. All Schiff bases found to be potentially active towards all microbial strains. The complexes contain $\mathbf{L_{12}}$ and $\mathbf{L_{14}}$ showed high activities against all bacterial strains and the complexes contain $\mathbf{L_{12}}$ and $\mathbf{L_{13}}$ showed promising results against all fungal strains[22].

Mallikarjun *et. al*., had synthesized lanthanum(III) complexes by reacting lanthanum(III) metal salt with Schiff bases derived from 3-substituted-4-amino-5-mercapto-1,2,4-triazole and glyoxal/ biacetyl/ benzyl. The analytical data and general behavior of the complexes suggest the empirical formula of the complexes as $LaLNO_3{\bullet}H_2O$, $LaLCl{\bullet}H_2O$ and $LaLNCS{\bullet}H_2O$. The IR and NMR spectra suggest dibasic tetradentate behavior of the ligands coordinating through the azomethine nitrogen and through the sulphur atom in thiol form of the ligand. IR spectral data indicate the coordination of nitrate, chloride and thiocyanate to the metal ion. All these observations taken together suggest that, a seven coordination around lanthanum(III) in the complexes of the type $LaLNO_3{\bullet}H_2O$ and lanthanum(III) ion exhibits coordination number six in the complexes of the type $LaLCl{\bullet}H_2O$ and $LaLNCS{\bullet}H_2O$. The lanthanum(III) complexes of the type $LaL_{15}NO_3{\bullet}H_2O$, $LaL_{16}NO_3{\bullet}H_2O$ and $LaL_{17}NO_3{\bullet}H_2O$ have shown moderate bacterial activity[23].

Kiran *et. al*., had synthesized metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) by the condensation of 4-amino-5- mercapto-3-methyl-s- triazole (AMMT), 4-Amino-3-ethyl-5-mercapto-s-triazole (AEMT) with 2-acetylpyridine. The structure of the complexes have been proposed by elemental analyses, spectroscopic data i.e. IR, ^{1}H NMR, electronic and magnetic measurements. Thermal studies of the complexes are also reported. Antibacterial activities of 10 complexes have been studied *in vitro*. Heterocyclic bidentate trazole Schiff bases were associated with substantially higher antibacterial activities than some commercial antibiotics. Out of 10 compounds tested, ApEMT-Co (1:1) and ApEMT-Co (1:2) were most active against all the four test bacteria at all the four

concentrations (500, 100, 50 and 10 μg ml^{-1}) showing maximum inhibition. The activities of the cobalt compound contain **L_{18}** was found more potent than some commercial antibiotics[24].

Muhi-Eldeenl *et. al*., had synthesized Ni(II), Co(II), Zn(I1) and Cd(I1) complexes of 3-mercapto-4-phenyl(cyclohexyl)-4H-1,2,4-triazoles. The new compounds were characterized by elemental analyses and spectroscopic techniques (IR, UV-Vis and ^{1}H NMR). *In vitro* antimicrobial activity of the complexes was determined against a variety of bacterial (Gram-positive and Gram-negative) and fungal species. The Ni, Co and Zn complexes exhibited little or no activity against the microbes, complexes of both the 4-phenyl 13 and 4-cyclohexyl 12 substituted triazoles were highly active as antifungal agents. Complex contain Ligands **L_{19}** and **L_{20}** significantly superior to the prototypical antifungal nystatin in inhibiting the growth of *Candida albicans* and *Candida pseudotropicalis*, showed equal effectiveness against *Saccharomyces cerevisiae*. The antibacterial activity of the Cd complexes was better than that observed for any of the other metal complexes, but generally not comparable to that of the reference antibiotic, streptomycin with the exception of the 4-cyclohexyl tiazole complex **L_{19}**, which was equivalent to streptomycin against *Staphylococcus aureus* and *Escherichia coli*[25].

Gangadhar *et. al.*, had synthesized a series of metal complexes of cobalt(II), nickel(II) and copper(II) by tetradentate 1,2, 4-triazole Schiff bases derived from the condensation of 3-substituted-4-amino-5-mercapto-1,2,4-triazole and 8-formyl-7-hydroxy-4-methylcoumarin. The metal(II) complexes exhibit coordination number six on the basis of magnetic and electronic spectral data having the stoichiometry of the type $(ML{\cdot}2H_2O)_2$. The metals are coordinated to azomethine nitrogen, lactonyl oxygen, phenolic oxygen and ulphur atom which had been confirmed by elemental analyses, spectroscopic measurements (IR, UV-vis, fluorescence, ESR), magnetic measurements and thermal studies. Electrochemical study of the complexes is also reported. All the complexes are soluble to limited extent in common organic solvents but soluble to larger extent in DMF and DMSO and are non-electrolytes in DMF and DMSO. All these Schiff bases and their complexes have also been screened for their antibacterial (*Escherichia coli, Staphylococcus aureus, Streptococcus pyogenes, Pseudomonas aeruginosa* and *Salmonella typhi*) and antifungal activities (*Aspergillus niger, Aspergillus flavus* and *Cladosporium*) by MIC method. All Schiff bases were found potentially active towards all microbial strains. Microbial studies of the metal(II) complexes contain ligands, **L_{21}**, **L_{22}** and **L_{23}** shows promising results. All Schiff bases found to be potentially active towards all microbial strains[26].

Sajjad *et. al*., had synthesized series of bidentate triazole-derived Schiff base ligands by the condensation reaction of 3,5- diamino-1,2,4-triazole with methyl-, chloro- and nitro substituted thiophene-2-carboxaldehydes in (1:2) molar ratio. The vanadyl(IV) sulphate ($VOSO_4.5H_2O$) in (1:2) (metal:ligand) molar ratio to prepare their oxovanadium(IV) complexes. Physical (magnetic and molar conductance), spectral (IR, NMR, electronic) and analytical (C, H, N and V %) data were evident that the Schiff base ligands are coordinated with the vanadium metal atom via azomethine-N and thienyl- S forming a square-pyramidal geometry. All compounds were tested against four Gram-negative (*E. coli, S. flexneri, P. aeruginosa, S. typhi*) and two Gram-positive (*S. aureus, B. subtilis*) bacterial strains. *In vitro* antifungal studies of all the compounds were carried out against *T. longifusus, C. albican, A. flavus, M. canis, F. solani* and *C. glabrata* fungal strains. The compounds contain **L_{24}**, **L_{25}** and **L_{26}** possessed overall significant (54–82 %) activity against all strains[27].

Altalbawy *et. al*., had synthesized triazole Schiff base with SNO donation sites, derived from condensation of 4-amino-5-phenyl-4H-1,2,4-triazole-3-thiol and salicaldehyde towards some bi- and trivalent metal ions, namely Cr(III), Mn(II), Fe(III), Co(II) (Cl, ClO_4), Ni(II) (Cl, ClO_4), Cu(II) and Zn(II). The chelates were found to have octahedral (Mn(II)), trigonal bipyramidal (Co(II),

Ni(II), Zn(II)) and tetrahedral (Cr(III), Fe(III) and Cu(II)) structures were characterized on the basis of elemental analysis, IR, ^{1}H NMR, solid reflectance, magnetic moment, molar conductance and thermal analyses (TG, DTG and DTA). The free Schiff base ligand and its metal complexes were tested *in vitro* against *Aspergillus flavus, Candida albicans, C. tropicalis,* and *A. niger* fungi and *Bacillus subtilis* and *Escherichia coli* bacteria in order to assess their antimicrobial potential. The compound Co(II) contain **L_{27}** showed a highest activity[28].

Mihaela *et. al*., had synthesized a series of complexes of type [ML(CH_3 COO)(OH_2)$_2$] (M: Co, Ni; HL: 2-[(E)-1H-1,2,4-triazol-3- ylimino) methyl]phenol)) and [M_2L_2(CH_3COO)$_2$ (OH_2)n] (M: Cu, n = 2; M: Zn, n = 0) by template condensation. The compounds were characterized with microanalytical, ESI–MS, IR, electronic, EPR spectra, thermal analyses, powder X-ray diffraction and magnetic data at room temperature. Based on the IR and ESI–MS spectra, a dinuclear structure with the acetate as bridge was proposed for Cu(II) and Zn(II) complexes. The antimicrobial activity of the obtained compounds was assayed on a large spectrum of microbial strains, i.e. Gram negative (*Escherichia coli ATCC 25922, E. coli 832, Klebsiella pneumoniae ATCC 134202, K. pneumoniae 806, Pseudomonas aeruginosa ATCC 27853*) and Gram positive (*Staphylococcus aureus MRSA 1263, S. aureus ATCC 25923, Bacillus subtilis ATCC 6633*) bacterial strains, as well as *Candida albicans* 22 fungal strain. The cobalt and copper compounds exhibited a broad spectrum of antibacterial activity towards both planktonic and biofilm-embedded cells. The antimicrobial assays revealed a very good antimicrobial activity for the obtained complexes, especially towards the Gram-negative bacterial strains (*E. coli* and *K. pneumoniae*), followed by *B. subtilis* and *C. Albicans strains*. The complex contain **L_{28}** exhibited the most evident anti-biofilm effect, inhibiting the biofilm development in the inert substratum, in case of the majority of the tested strains, being promising agents for the development of new antimicrobial agents and surfaces[29].

Prakash *et. al*., had synthesized lanthanum(III) complexes by reacting lanthanum(III) nitrate with triazole Schiff bases derived from 3-substituted-4-amino-5-hydrazino-1,2,4-triazole and substituted salicylaldehydes. All these complexes are soluble in DMF and DMSO and the low molar conductance values observed indicates that they are nonelectrolytes. 1,2,4-triazole Schiff bases act as dibasic tetradentate ligands through the coordination of azomethine nitrogen and phenolic oxygen atoms to the metal ion. The bonding of ligands to metal ion was confirmed by the elemental analyses, analytical, IR, PMR, TGA and fluorescence data. The complexes were evaluated for their biological activity. It was observed that the representative ligand (II) is highly active against *E. Coli, S. aureus* (bacteria) and *A. Niger* (Fungi); whereas lanthanum (III) complex with ligand **L_{29}** show high activity only against *E. Coli*[30].

Prakash *et. al*., had synthesized a series of Co(II) complexes with Schiff bases derived from 3-substituted-4-amino-5-hydrazino-1,2,4-triazole and substituted salicylaldehydes. The Synthesized Schiff bases act as tetradentate ligands in the sequence of ONNO through the coordination of azomethine nitrogen and phenolic oxygen atoms to the metal ion. The bonding of ligands to metal ion was confirmed by the analytical, IR, ^{1}H-NMR, electronic, magnetic, FAB-mass, fluorescence, thermal studies solid-state DC electrical conductivity and molar conductance data. The Schiff base shows higher activity than the other compounds against *E. coli* and *S. aureus* and among the Co(II) complex (**L_{30}**) exhibits relatively high activity against *A. niger*[31].

Anjali *et. al*., had synthesized 4-diazo-5-mercapto-3-methyl/ethyl-s-triazoles were coupled with active methylene groups viz: acetyl acetone, ethylcyanoacetate and malanodinitrile to get dinucleating ligands. These ligands were reacted with Ni(II) and Cu(II) chlorides. Dinucleating ligands and metal complexes were characterized by elemental analysis, IR, NMR, ESR and magnetic movement studies. On the basis of physico-chemical studies Ni(II) and Cu(II) complexes have been

assigned octahedral structure. The synthesized compounds have been screened for their antimicrobial activity. In accordance with this synthesized compounds and their metal complexes were examined for antimicrobial assay against 8 bacteria [*Bacillus subtilis, Ervinia carotovora, Pseudomonas vulgaris, Escherichia coli, Enterococcus faecalis, Streptococcus faecalis, Klebsilia pneuomonia, Micrococcus luteus*] and 4 fungi [*Asprgillus flavus, Pencillian expasom, Lasiodiplodia theobroma, Rhizoctonia solani*] Moreover Cu complexes showed more activity against all bacteria. **L_{31}**-Cu showed good microbial activity[32].

Mallikarjun *et. al*., had synthesized a series of copper(II) complexes of Schiff bases derived from 3-substituted-4-amino-5-mercapto-1,2,4-triazole and glyoxal/biacetyl/benzyl have been synthesized and characterized on the basis of analytical and spectroscopic studies. The elemental analysis agrees well with the 1:1 stiochiometry of the type $ML(H_2O)$, with L coordination via the two imine nitrogen and two thiolato sulphurs in an overall octahedral geometry. Some of the complexes were screened for their antibacterial and antifungal activity and copper(II) complexes with **L_{32}** are more active than the free Schiff bases[33].

Mahasin *et. al*., had synthesized some transition metal complexes Cr (III), Ni (II), Cd (II) and V (IV) Complexes of olefinic bistriazole as a ligand. The prepared complexes were identified and their structural geometries were suggested by using Flame Atomic Absorption technique, FT-IR and UV-Visible Spectrophotometer as well as to Magnetic Susceptibility and Conductivity measurement. Semi-empirical methods (PM3 and MINDO/3) were carried out to evaluate the vibration frequencies, heat of formation ($\Delta H^{o}f$) and binding energy (ΔEb) for all metal complexes. The ligand behave as a tetradentate chelating with two sulfur atoms and two olefinic groups, to form an octahedral geometry for the chromium and nickel complexes and a tetrahedral geometry for the cadmium complex, in addition to square pyramid for the vanadium complex. And it is also studying their biological activity against two selected microorganisms (*pseudomonas aeruginosa* and *staphylococcus aureus*). Cr-Ligand (**L_{33}**) shows highest activity for all strains[34].

Madhu *et. al*., had synthesized complexes of Mn(II), Fe(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Pd(II) with 4-{(E)-[1-(1H-benzo[d]imidazol-2-yl)ethylidene]amino}-3-methyl-1H-1,2, 4-triazole-5(4H)-thione (Hbzeamt) and with 4-{(E)-[1-(1H-benzo[d]imidazol-2-yl)phenylmethyleneamino)-3-methyl-1H-1, 2, 4-triazole-5(4H)-thione (Hbzpamt) of composition [ML2] (M= Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II), HL= Hbzeamt or Hbzpamt), PdLX (L= Hbzeamt or Hbzpamt and X= Cl or Br) and $[M(LH)Cl_2]$ (M= Co(II), Ni(II), or Cu(II)). The proposed structures of all the synthesized compounds were studied using elemental analysis, UV, IR, magnetic susceptibility ^{1}H-NMR and mass spectroscopy. All compounds were evaluated for antibacterial activity (*E. coli, S. aureus* and *Salmonella typhi*) and the antifungal activity (*A. niger, A. flavus* and *R. Phaseoli*). The antifungal and antibacterial activity of Cu(II) and Co(II) complexes were higher than free ligands and other metal complexes[35].

Ramasubramanian *et. al*., had synthesized a series of transition metal - triazole derivatives. Octahedral structures have been proposed for Co(II) and Ni(II) complexes square planar geometry for Pd(II) complex and tetrahedral structure for Zn(II). Zn(II), Co(II) and Ni(II) complexes characterized by microanalytical, thermal, magneto-chemical and spectral studies. The complexes of Co(II) contain **L_{34}** emerged as a good antibacterial agent against Gram-negative bacteria such as *Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Bacillus subtilis* and *Shigella flexneri*[36].

Parekh *et. al*., had synthesized 1-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-chloroethanone was condensed with 5-amino-2-hydroxy benzoic acid (5-Amino Salicylic acid). The resulting 5-(2-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-oxoethylamino)-2-hydroxy benzoic acid was characterized by elemental analysis and spectral studies. The transition metal chelates of the same

were prepared with Cu^{2+}, Ni^{2+} , Co^{2+} , Mn^{2+} and Zn^{2+} and characterized by IR spectral studies and magnetic properties. The antimicrobial activity of ligand and its metal chelates were screened against various gram-positive and gram-negative organisms. The results show that all these samples are more or less active agents against various organisms. The ligand molecule (**L_{35}**) acts as a tetra dentate ligand in all the studied cases of complex. Octahedral structures for Ni (II), Co (II), and Mn (II) complexes, tetrahedral polymeric structure for Zn (II), and distorted octahedral for Cu (II) complex have been tentatively proposed. The result indicates that the Cu (II) and Zn (II) complexes contain **L_{35}** exhibits higher activity towards most of the plant pathogenic organisms studied than the ligand[37].

Sreedhar *et. al*., had synthesized A $[Ru_2L]^{4+}$ ruthenium(II) triply-stranded helicate was synthesized from a bis-bidentate "click" pyridyl-1,2,3-triazole ligand and $RuCl_3$ in good yield (58%). The new complexes were characterized by elemental analysis, IR, UV-vis, ^1H, ^{13}C and ^1H DOSY NMR spectroscopies and the molecular structure confirmed using X-ray crystallography. Compounds were tested for antimicrobial activity in vitro against both Gram positive (Staphylococcus aureus) and Gram negative (Escherichia coli) microorganisms by Agar-based disk diffusion assays indicated that the Ru(II) helicate displayed antimicrobial activity but the minimum inhibitory concentrations (MIC) proved to be extremely modest (MIC > 256 μg/mL)[38].

Creaven *et. al*., had synthesized Cu(II) and Zn(II) complexes of quinolin-2(1H)-one-triazole derived Schiff base by the condensation of 4-amino-1,2,4-triazole with *N*-substituted-3-formyl-4-hydroxyquinolin-2-(1H)-one derivatives. The complexes were characterized by standard techniques and for two of the complexes X-ray crystallography confirmed that the geometry at the metal centre was octahedral in both cases and that the Schiff base acted as a bidentate ligand coordinating to the metal(II) ion through the deprotonated oxygen and azomethine nitrogen atoms. All of the compounds were investigated for their antimicrobial activities against a fungal strain, *Candida albicans*, and against Gram-positive and Gram-negative bacteria. The compounds were found to be active against *C. albicans* but inactive against Staphylococcus aureus and Escherichia coli. In this work, none of the Schiff base ligands and their metal(II) complexes showed bacterial growth inhibition at maximum concentrations of 200 μM which were found to exhibit good antifungal activity. Zn(II) complexes contain **L_{36}** showed increased activity compared to the corresponding free ligands[39].

Sumrra *et. al*., had synthesized a series of new triazoles and their oxovanadium(IV) complexes by the condensation reaction of 3,5-diamino-1,2,4-triazole with 2-hydroxy-1-naphthaldehyde, pyrrole-2- carboxaldehyde, pyridine-2-carboxaldehyde, 2-acetyl pyridine and 2-methoxy benzaldehyde. The structures of the compounds had been established and proposed to have a square pyramidal geometry on the basis of their physical, spectral (IR, ^1H and ^{13}C NMR and mass spectrometry) and elemental analytical data. The ligands and their complexes were screened for in vitro antibacterial activity against six bacterial species such as, *Escherichia coli, Shigella flexneri, Pseudomonas aeruginosa, Salmonella typhi, Staphylococcus aureus* and *Bacillus subtilis* and for *in vitro* antifungal activity against six fungal strains, *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani and Candida glabrata*. The oxovanadium(IV) complex contain **L_{37}**, **L_{38}** and **L_{39}** showed significant activity against all bacterial and fungal strains[40].

Calu *et. al*., had synthesized series of complexes $[M_2L_2Cl_2(OH_2)n]mH_2O$ (M: Co, n = 0, m = 1; M: Ni, n = 2, m = 0; M: Cu, n = 0, m = 0; M: Zn, n = 0, m = 1; HLH_2O: 2-[(E)-1H- 1,2,4-triazol-3-ylimino)methyl]phenol). The features of complexes have been assigned from microanalytical, thermal, IR, UV–Vis-NIR, EPR spectroscopy, powder X-ray diffraction, TG/DTA and cyclic voltammetry as well as magnetic data at room temperature. The complexes exhibited an improved antibacterial activity in comparison with the ligand towards both

planktonic as well as biofilm embedded cells. The most active compounds against planktonic cells were the Cu(II) and Zn(II) complexes, while Co(II) complex with Ligand **L_{40}** inhibited the biofilm formed by the majority of the tested strains, demonstrating its utility for the design of novel materials and strategies for fighting against medical biofilms and associated chronic infections[41].

Said Amer *et. al*., had synthesized A series of copper (II) complexes of Schiff bases derived from 4H-3,5-diamino- 1,2,4-triazole with 2-pyridinecarbaldehyde, salicylaldehyde, 2,4-dihydroxybenzaldehyde and 2-hydroxy-1-naphthaldehyde. The donor atoms and the possible geometry of the complexes were investigated by means of elemental and thermal analyses, molar conductance, magnetic moment, UV–Vis, IR, ESR and mass spectra. The ligands behaved as tetradentate, coordinating through the nitrogen atom of the azomethine group and the nearest nitrogen atom to it or oxygen atom of a-hydroxyl group. The spectral studies confirmed a four coordinate environment around the metal ion. These complexes were also tested for their *in vitro* antimicrobial activities against some bacterial and fungal strains. The results of the antibacterial activity of the tested ligands and their complexes showed moderate activity against E. *coli* and *S. aureus* when compared with the standard drug, tetracycline[42].

Ajaykumar *et. al*., had synthesized the Co(II), Ni(II), and Cu(II) complexes with Schiff bases derived from 3-substituted-4-amino-5-mercapto-1,2,4-triazole and fluvastatin have been synthesized. Schiff bases exhibited thiol-thione tautomerism and coordinated to metal ion through azomethine nitrogen and thiolate sulphur atoms. Square planar geometry for all the metal complexes of the type ML_2 has been proposed in the light of analytical, spectral (IR, UV–Vis., ESR, and FAB mass), magnetic, and thermal studies. The antimicrobial studies of Schiff bases and their metal complexes against various antibacterial (*Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Bacillus subtilis*) and antifungal (*Aspergillus niger* and *Pencillium Chrysogenum*) species by Minimum Inhibitory Concentration method revealed that, the metal complexes possess more healing antibacterial activity than the Schiff bases. Complex Co-$(L_{41})_2$ showed good activity[43].

Vidyavati Reddy *et. al*., had synthesized Coordination complexes of Cu(II),Co(II), Ni(II), Mn(II) and Fe(III) with Schiff bases derived from 3-(4-chlorophenoxymethyl)-4-amino-5- mercapto-1, 2, 4-triazole and substituted aldehydes. The complexes were characterized by elemental analysis, conductivity measurements, magnetic susceptibility data, electronic, IR, ESR and ^{1}H NMR spectral data. On the basis spectroscopic studies, the Schiff base is monobasic bidentate ligand having the composition $ML_2(2H_2O)$ Where M = Cu(II), Co(II), Ni(II) ,Mn(II), $ML_2(H_2O)Cl$ Where M = Fe(III). Various physicochemical data suggest a six coordinated octahedral geometry for Cu(II),Co(II), Ni(II), Mn(II) and Fe(III) complexes. The antibacterial activities of ligand and its complexes were screened by cup plate method. The ligand 2-[(E)-({3-[(4-chlorophenoxy) methyl]-5-mercapto-4H-1, 2, 4-triazol-4-yl} imino] phenol behaved as a monobasic bidentate coordinating through 'N' and 'O' of OH group. The ligand **L_{42}** and its Cu(II) and Co(II) complexes shows weak activity when compared to the standard drug, clotrimazole[44].

Patil *et. al*., had synthesized a series of Mn(II), Fe(III) and Zn(II) complexes have been synthesized with Schiff bases derived from isatin and 3-substituted-4-amino-5-mercapto-1,2,4-triazole. The elemental, spectroscopic (Infrared, nuclear magnetic resonance, ultraviolet-visible, fast atom bombardment-mass, fluorescence and electrochemistry) and magnetic studies suggested that the metal complexes possess octahedral geometry. The Schiff bases and their metal complexes exhibit fluorescent properties. The antimicrobial studies of Schiff bases and their metal complexes against various bacterial and fungal species by the minimum inhibitory concentration method revealed that the metal complexes possess more healing antibacterial activities than the Schiff bases. In particular complex with **L_{43}** showed higher activity than the respective[45].

Anti-Cancer Activity

Currently, the treatment for cancer primarily includes surgery and chemotherapy, but the curative effects of the existing chemotherapeutic drugs are not good enough and they have plentiful side effects. The development of more effective drugs for treating patients with cancer has been a main attempt over the past 50 years.

Brine shrimp bioassay was carried out for in vitro cytotoxic properties against Artemia salina. Two compounds **L_4** and **L_6** showed potent cytotoxic activity against Artemia salina, while all other compounds were considered inactive for cytotoxic bioassay[18]. *In vitro* Brine Shrimp bioassay was also carried out to investigate the cytotoxic properties of these compounds. The data also revealed that the metal complexes showed better activity than the ligands due to chelation/coordination. All compounds were considered as almost inactive in this assay[20]. The brine shrimp bioassay was also carried out to study their in vitro cytotoxic properties. The complexes containing **L_{12}**, **L_{13}** and **L_{14}** displayed potent cytotoxic activities as LD_{50} = 7.439×10^{-4}, 8.974×10^{-4} and 8.945×10^{-4} M ml^{-1}, respectively, against *Artemia salina*, while all other compounds were almost inactive for this assay[22]. The brine shrimp bioassay was also carried out to study their *in vitro* cytotoxic properties. Cytotoxic activity was observed that complex contain **L_{21}**, **L_{22}** and **L_{23}** displayed weak cytotoxic activity against *A. salina,* while the other compounds gave values of LD_{50} therefore can be considered non-cytotoxic[26].The cytotoxicity evaluation of ligand and complexes solution in DMSO was performed on human tumor cell line Hep 2 (human laryngeal carcinoma).The complexes with Ligand, **L_{28}** exhibit a low cytotoxicity except for Cu(II) species that induces the early apoptosis for the HEp 2 cells[29]. Cytotoxic nature of the compounds was reported using brine shrimp bioassay method against Artemia salina. The recorded data clearly indicated that only the oxovanadium complexes showed potent cytotoxicity rather than their non-coordinated ligands[39]. The cytotoxicity evaluation of the ligand and the obtained complexes was performed on two human tumour cell lines, i.e. Hep 2 (human cervix carcinoma HeLa derivative) and HCT 8 (human ileocecal adenocarcinoma), respectively. The Cu(II) and Zn(II) complexes with **L_{40}** exhibited an inhibitory effect on the tumour cell lines growth, as revealed by the increased G2 phase and percentage of apoptotic/necrotic cells[41].

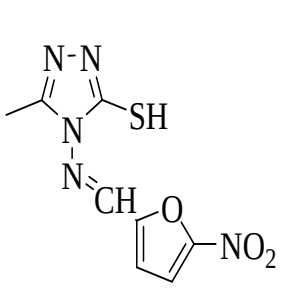
Alias *et. al*., had synthesized two new complexes with formula [M(NMP. (5-(4-Nitro Phenyl)-4-Amino-3-Mercapto Propenyl-1,2,4-Triazole))$(H_2O)_3$]$(NO_3)_2$.3EtOH (where M is Ni and Co(II) ions respectively, NMP. These complexes have been characterized by spectroscopic methods such as (ultraviolet- visible and infrared), as well as to thermal gravimetric, metal analyses, microanalyses, conductivity, magnetic moment and molar ratio method. To measure the biologic activity and potential anticancer efficacy of these compounds, they have been compared with cisplatin on human hepatocarcinoma HepG2 cell lines in different eight concentrations (2000, 1000, 500, 250, 125, 62.5, 31.25 and 15.625 μg/ml) respectively, in the time of exposure 72 hrs. The results exhibit that the three prepared complexes i.e. ligand (NMP.TRZ) and its metal complexes have shown higher ratios cytotoxicities compared to cisplatin against HepG2 cell lines in most selected concentrations. Based on the obtained results of biological test, these compounds with **L_{44}** may be potentially being considered as good anticancer candidates for further pharmacological studies[46].

Other Biological Activity

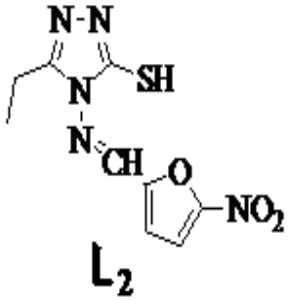
The binding modes of the complexes with DNA have been investigated by UV-Vis absorption titration. The results showed that the mode of binding of the complexes to DNA is intercalative or non-intercalative binding modes[17]. Co(II), Ni(II), and Cu(II) complexes cleave the DNA isolated from *A. niger*. On the basis of spectroscopic results, the square planar geometry is proposed for all the newly synthesized complexes. All these complexes cleaved the DNA of *A. niger*[18]. DNA cleavage property of Mn(II), Fe(III) and Zn(II) complexes revealed the important role of metal ion in the biological system. Mn(II) and Zn(II) complexes exhibited the DNA

cleavage property against the DNA isolated from the *S. aureus* bacterial species whereas the Mn(II), Fe(III) and Zn(II) complexes cleave the DNA isolated from *A. niger*[45].

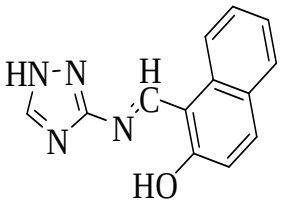
Anthelmintic assay was performed on adult Indian earthworms (Pheretima posthuma), due to its anatomical and physiological resemblance with the intestinal roundworm parasite of human beings. Among the Mn(II), Fe(III) and Zn(II) complexes, the complexes of Mn(II) showed more antheminitic activity and the remaining Fe(III), Zn(II) complexes and Schiff bases are less active. Thus, the biological studies revealed the important role of metal ions in the biological systems[45].



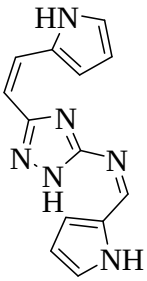
L_1



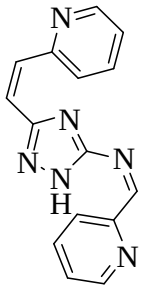
L_2



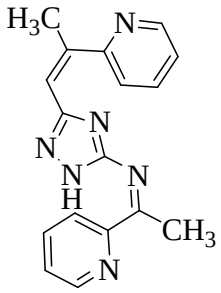
L_3



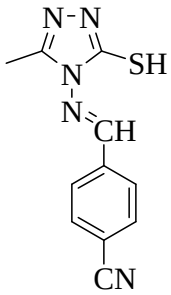
L_4



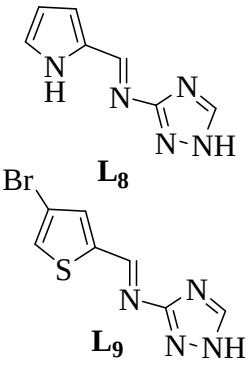
L_5



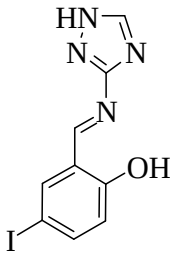
L_6



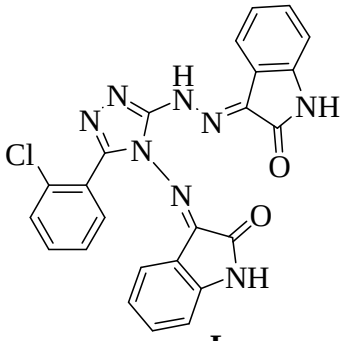
L_7



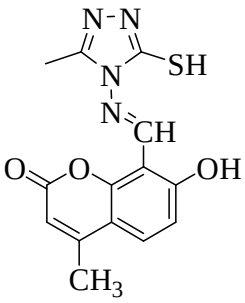
L_8 **L_9**



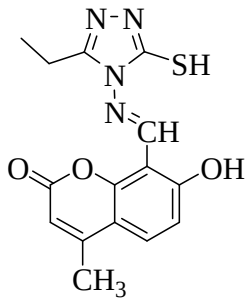
L_{10}



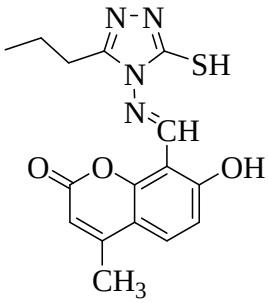
L_{11}



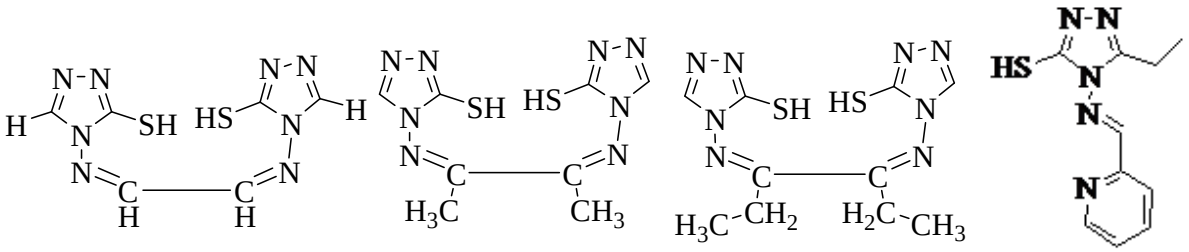
L_{12}



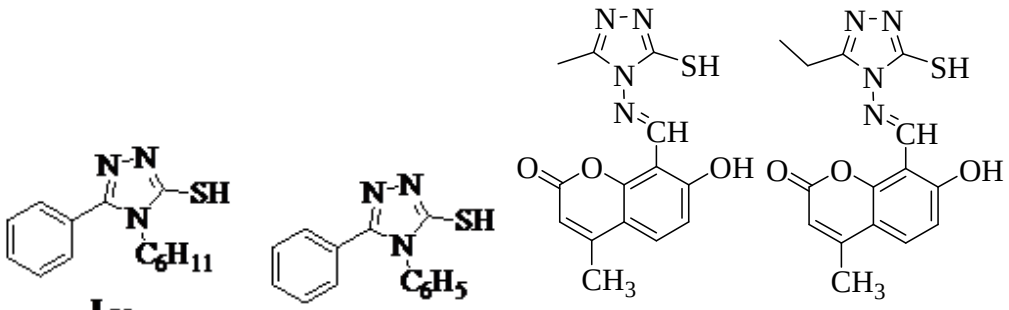
L_{13}



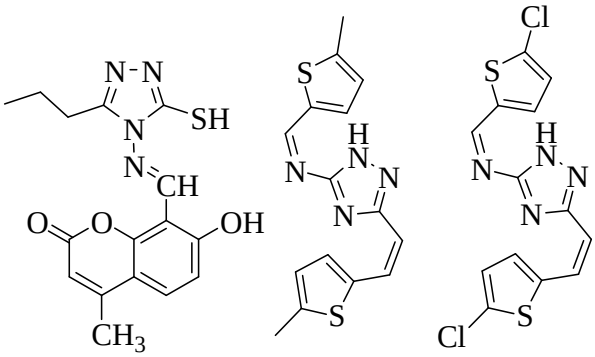
L_{14}



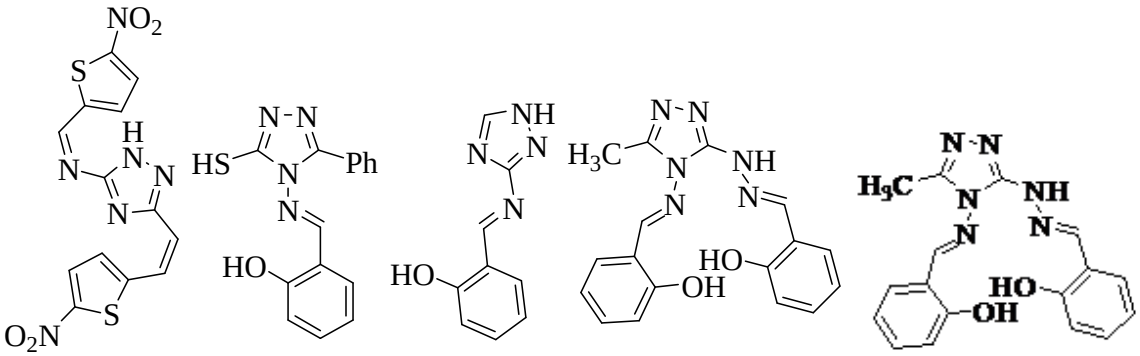
L_{15} **L_{16}** **L_{17}** **L_{18}**



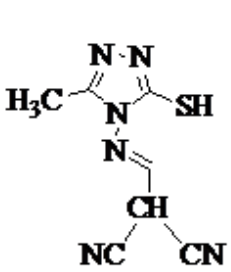
L_{19} **L_{20}** **L_{21}** **L_{22}**



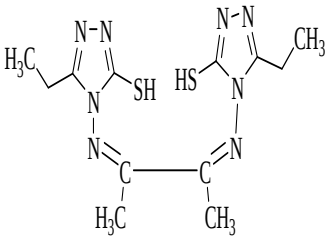
L_{23} **L_{24}** **L_{25}**



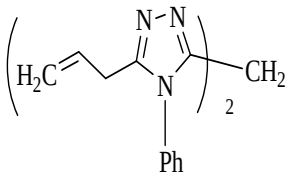
L_{26} **L_{27}** **L_{28}** **L_{29}** **L_{30}**



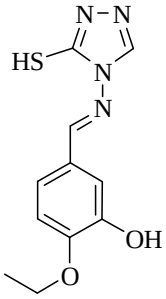
L_{31}



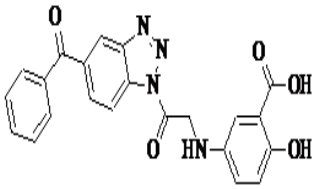
L_{32}



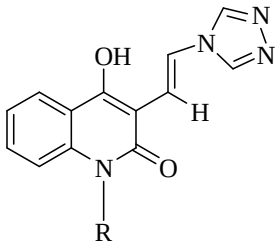
L_{33}



L_{34}

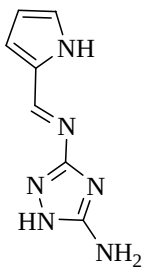


L_{35}

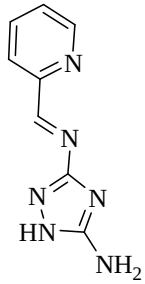


R = H, CH_3, C_2H_5

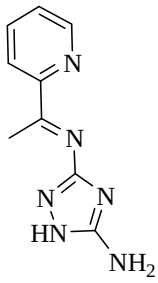
L_{36}



L_{37}



L_{38}



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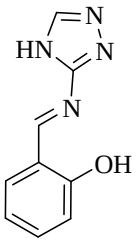
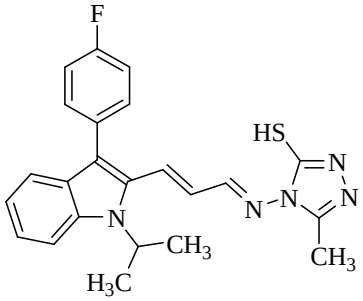
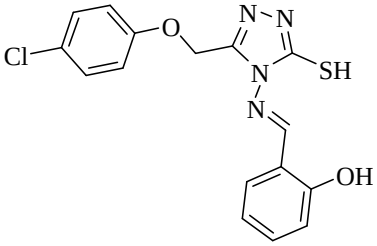


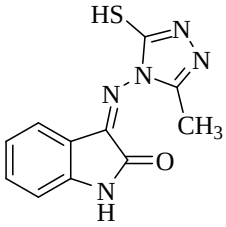
L_{40}



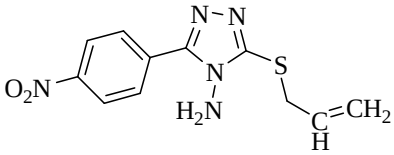
L_{41}



L_{42}



L_{43}



L_{44}

CONCLUSION

In the field of medicinal chemistry, the role of transition metal complexes as therapeutic compounds is becoming increasingly important. Recent development in medicinal chemistry has made possible formation of number of metal complexes with triazole ligand of interest, which can be used as therapeutic agent. Significant progress in the synthesis of copper based anti-microbial drugs has been made. These drugs have proven to be highly effective chemotherapeutic agents. These metal complexes offer a great diversity in their action; they do not only have anti-microbial properties but have also been used as anti-cancer, DNA Cleavage, anthemintic compounds. Development of metal complexes as drugs is not an easy task; considerable effort is required to get a compound of interest. Besides all these limitations and side effects, metal

complexes are still the most widely used chemotherapeutic agents. It makes a large contribution to medicinal therapeutics in a way that was unimaginable last ten years back.

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