ejpmr, 2018,5(6), 192-206

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

BIOLOGICAL POTENTIAL OF HETEROCYCLIC TRANSITION METAL COMPLEXES: A REVIEW

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Article Received on 30/03/2018 **Article Revised on 20/04/2018** **Article Accepted on 10/05/2018**

ABSTRACT

Transition metal complexes play an important role in medicinal inorganic chemistry. Due to the metal chelation, these compounds have attracted much attention in the development of new drug discovery. The use of heteroaryl ring system in metal chelation have attracted considerable attention owing to their unique properties as pH-sensitive, photochromic, rodox responsive, stabilizes low valent metal oxidation states etc. The heterocyclic ligands and their metal complexes can be used as antimicrobial, antitumor, antihistaminic, antioxidative, anti-inflammatory, analgesic and neuroprotective properties. The present review complies the recent progress in the biological activities of transition metal complexes bearing heterocyclic ligands.

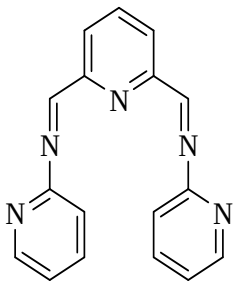
KEYWORDS: Anticancer, Antimicrobial, Heterocyclic ligands, Metal complexes.

INTRODUCTION

Transition metal complexes have attracted considerable attention owing to their fascinating chemical and physical properties, and their wide-ranging applications in medicine.[1] The integration of metal with organic compound can produce well diversified structures with pronounced biological activities due to chelation.[2,3] The presence of heteroaryl ring systems have numerous benefits due to their unique properties as pH-sensitive, photochromic, redox responsive, stabilizes low valent metal oxidation states. Several reports also showed that metal complexes show higher activity than the parent ligands.[4-5] The metal complexes prepared from heterocyclic ligands can be used as antifungal, anti-inflammatory, anti-HIV, anticancer, diuretic, hypoglycemic, antithyroids, and antimalarials etc.[6,7] In view of this; the present review aims to summarize the recent progress in the biological potential of transition metal complexes bearing heterocyclic ligands.

Biological activities of heterocyclic transition metal complexes

The synthesis of a Schiff base ligand **(1)**, via condensation of pyridine-2,6-dicarboxaldehyde with 2-aminopyridine, and its transition metal complexes have been reported by *H.F.A. El-halim et al*.[8] The synthesized ligand and its metal complexes were screened for antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus pyogones* where the activity data shows that the metal complexes to be more potent than the parent ligand. *M. Gaber et al*[9] have reported the synthesis of Schiff base ligand, the condensation product of 3-amino-1,2,4-triazole with 2-hydroxy-1-naphthaldehyde, and its Ni(II), Pd(II) and Pt(II) metal complexes **(2)** and evaluated for their moderate activity towards the *E. coli* and *S. aureus* bacteria. Furthermore, the ligand exhibited stronger antitumor activity while its Pd(II), Pt(II) and Ni(II) complexes exhibited a weak antitumor activity against HEPG2 cell.



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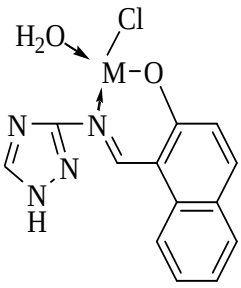

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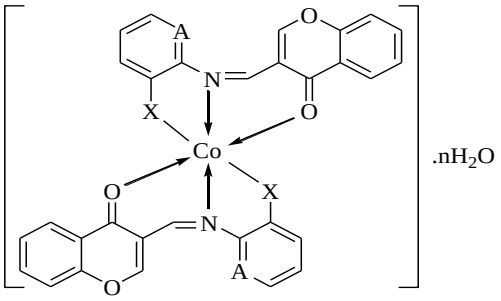
A sequence of Co(II) complexes **(3)** of formyl chromone Schiff bases have been synthesized, characterized and screened for various biological activities by *P. Kavitha et al*.[10] The activity data showed that Co(II) complexes have greater antimicrobial activity than ligands. All ligands and Co(II) complexes showed considerable anticancer activity against Raw, MCF-7 and COLO 205 cell lines however considerably moderate to less pronounced compared to the standard drug cisplatin. Cu(II), Zn(II) and Pt(II) metal complexes **(4)** of NSAID piroxicam drug have been synthesized and characterized

by spectroscopic and analytical techniques and examined the effect of proliferation of complexes on the HeLA and C6 cells using real-time cell analyzer with four different concentrations.[11]



A = C and X = O/S/COO
A = N and X = O

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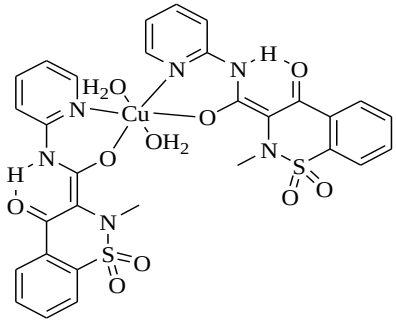

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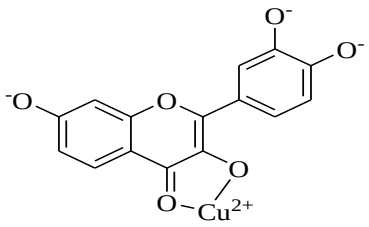
The plant polyphenol, Fisetin (3,3′,4′,7-tetrahydroxyflavone) metal chelates revealed to be broad prospects for the treatment of various diseases. *E. Łodyga-Chruscińska et al*[12] have reported the Cu(II)-fisetin complexes **(5)** and investigated significant DNA cleavage activity, followed by complete degradation of DNA. The *in vitro* antioxidant and pro-oxidant activity of Cu(II)-fisetin complexes have been studied using DPPH, ABTS and mitochondrial assays. Furthermore Cu(II)-fisetin complexes were screened for their antimicrobial activity and antagonistic activity. *W.H. Mahmoud et al*[13] have synthesized a series of transition metal complexes **(6)** of (Z)-4-(1-((2-carboxycyclohexa-2,4-dien-1-yl)imino)-ethyl)[bis(h5-cyclopenta-1,3-dien-1-yl)]iron mixed with 1,10-phenanthroline. The mixed ligand complexes were screened against pathogenic antibacterial and antifungal strains. Besides, the anticancer activity against the breast cancer cell line MCF7 was studied and found to have moderate results.



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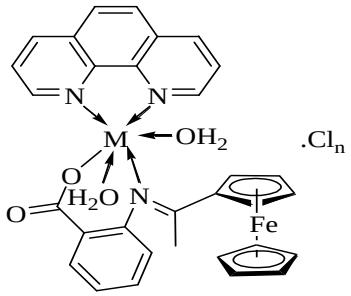
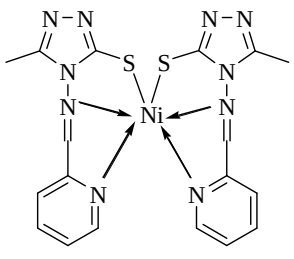


6

A.-N.M.A. Alaghaz et al[14] have derived Schiff base, from condensation of s-triazole (4-amino-5-mercapto-3-methyl-S-triazole) with pyridine-2-aldehyde, and their corresponding Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes **(7)** and evaluated for their antifungal activities against *Aspergillus niger*, *Fusarium solani* and *Candida albicans*. Additionally, *A.-N.M.A. Alaghaz et al*[15] have synthesized and characterized the azo-dye complexes **(8)** of 4-(4-hydroxy)-3-(2-pyrazine-2-carbonyl) hydrazonomethylphenyl-diazenyl-benzenesulfonamide with Mn(II), Co(II), Ni(II), Zn(II) and Cd(II) and screened against various fungi. Further, the docking experiments indicate that these complexes showed high binding score with active site of enzyme help designing novel potent CAII inhibitors.



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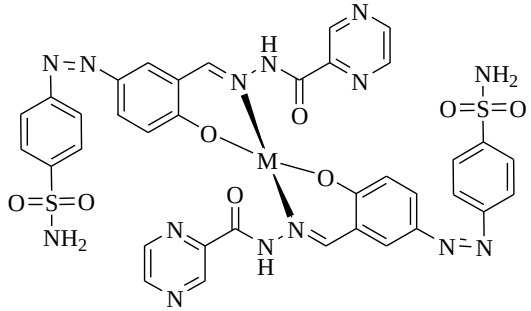

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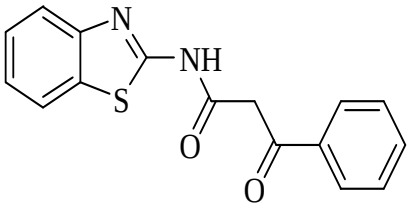
N.E.A. El-Gamel et al[16] have synthesized Ni(II) and Mn(II) complexes of N-(benzo[d]thiazol-2-yl)-3-oxo-3-phenylpropanamide **(9)** as potent antimicrobial agents. Mn(II) complex showed moderate antimicrobial activity while Ni(II) complex displayed a promising activity against *Candida albicans* and *Staphylococcus aureus*. 2-(*o*-Sulfamoylphenyl) benzimidazole **(10)** coordinated with the divalent transition metals Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) were synthesized and characterized by *A.W.A. Siddiqui et al*.[17] The ligand and its metal complexes were evaluated for their potential antimicrobial activity against a range of bacterial and fungal strains.



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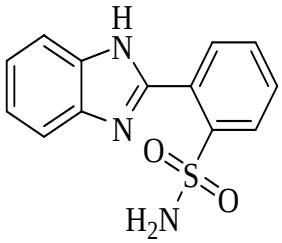

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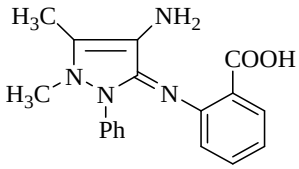
M.M. Omar et al[18] have reported a novel antipyrine Schiff base ligand **(11)**, prepared via condensation of 4-aminoantipyrine and 2-aminobenzoic acid, and their metal complexes and were screened for their antibacterial activity against bacterial species, *Escherichia Coli*, *Pseudomonas aeruginosa*, *Staphylococcus Pyogones* and *Fungi* (Candida). The activity data indicate that the metal complexes showed more potent antibacterial than the Schiff base ligand. *O.A. El-Gammal et al*[19] have synthesized and characterized a new series of transition metal complexes from 2-acetylpyridine-a-naphthoxyacetylhydrazone **(12)**. Moreover, the ligand and its complexes were screened against antibacterial, antioxidant using DPPH radical and antitumor activities using *in vitro* Ehrlich ascites assay. The activity data result showed that Cd(II) and Mn(II) complexes proved to have the highest cytotoxic activity while Co(II) complex have the moderate cytotoxic activity comparable to standard drug.



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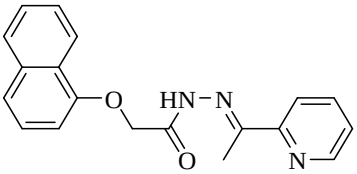
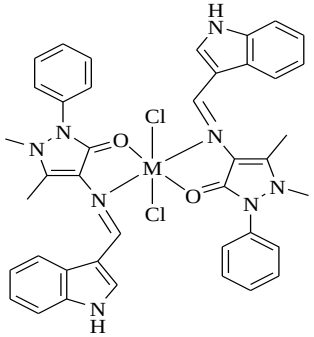


12

Co(II), Ni(II), Cu(II) and Zn(II) Complexes **(13)** of the Schiff base ligand, derived from indole-3-carboxaldehyde and 4-aminoantipyrine, were synthesized and characterized by *M.S. Nair et al*.[20] The *in vitro* biological screening effects of the complexes were tested against various microbial species and the results indicate that the Ni(II) and Co(II) complexes showed better activity against most of the microbial species compared to that of ligand and other complexes. The DNA cleavage studies indicate that the Ni(II), Cu(II), and Zn(II) complexes have completely cleaved the DNA. J. Sahoo and S.K. Paidesetty[21] have evaluated bis[{4-((4-bromo-3-methyl-phenyl)diazenyl)- 2-((4-phenylthiazol-2-limino)methyl)phenoxy}]Co(II), and bis[4-{(4-bromo-3-methylphenyl) diazenyl}-2-{(4-(4-chlorophenyl) thiazol-2-ylimino)methyl} phenoxy]Co(II) **(14)** for their significant antioxidant and improved radical scavenging activities.



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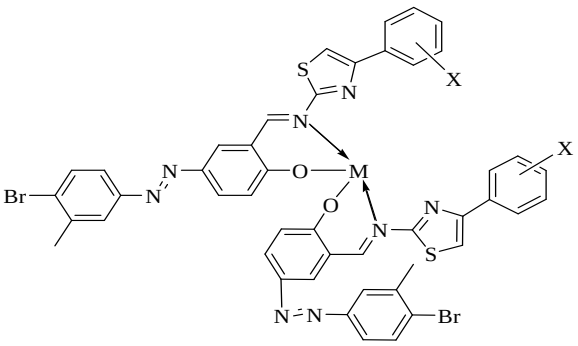
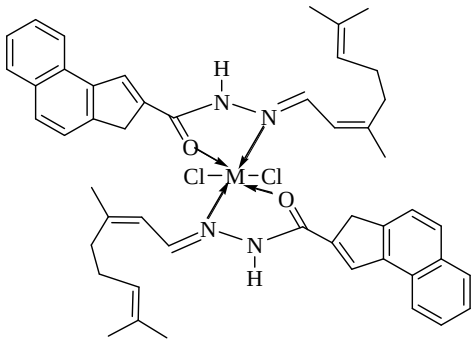


14

M.B. Halli et al[22] have synthesized a series of Co(II), Ni(II), Cu(II), Cd(II), Zn(II) and Hg(II) complexes **(15)** of citral-naphthofuran-2-carbohydrazide Schiff base. The free ligand and their metal complexes were evaluated for their antioxidant activity, *in vitro* antibacterial activity and antifungal activities. In addition, the DNA cleavage studies of all the complexes were studied by agarose gel electrophoresis method. The mycological studies showed that all the complexes are superior to the free ligand and their toxicity has increased upon chelation. *C.T. Prabhakara et al*[23] have synthesized the Co(II), Ni(II) and Cu(II) complexes **(16)** of Schiff bases, derived from 8-formyl-7-hydroxy-4-methylcoumarin/3-chloro-8-formyl-7-hydroxy-4-methylcoumarin with 2,4-difluoroaniline/o-toluidine respectively. The synthesized Schiff bases and their metal complexes were screened for promising antibacterial, antifungal, anthelmintic and DNA cleavage activities.



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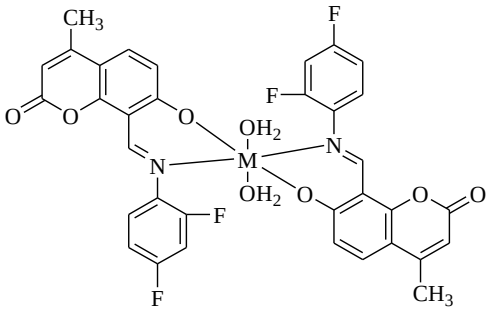
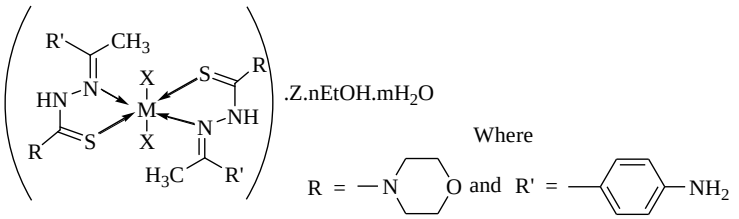


16

E.A. El-Samanody et al[24] have synthesized a new series of Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) complexes **(17)** derived from (*E*)-N'-(1-(4-aminophenyl)ethylidene)morpholine-4-carbothiohydrazide and screened for *in vitro* the molluscicidal effect on the mucous gland of Eobania vermiculata. The tested compounds have almost same and significant toxic effect of metaldehyde which increases the mucous secretion of the snails and leads to death. Hence, these can be used to combat the proliferation of Eobania vermiculata. Furthermore, *E.A. El-Samanody et al*[25] have synthesized a new series of some biologically active Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) complexes **(18)** from the novel thiosemicarbazone ligand; (E)-N'-(furan-2-ylmethylene)morpholine-4-carbothiohydrazide. The ligand and its complexes were screened *in vitro* for their molluscicidal activity against *Eobania vermiculata*. Accordingly, this set of new compounds may be used as anti-molluscicidal agents to combat the proliferation of these pests.



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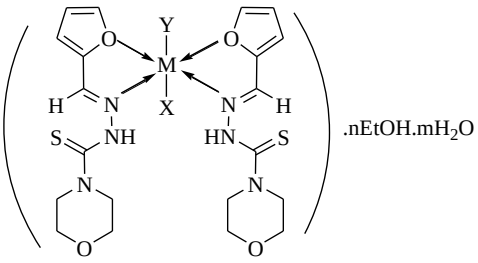
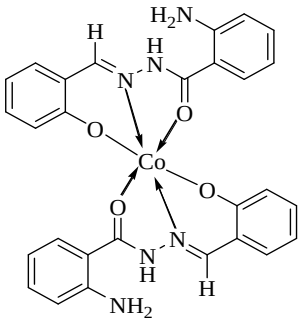


18

D.S. Badiger et al[26] have reported the synthesis of transition metal complexes **(19)** of salicylhydrazone of anthranilhydrazide and screened for their antimicrobial activity. The activity data showed that the metal complexes have superior antibacterial and antifungal activity than the free ligand. Additionally, the metal complexes were also tested against the *M. tuberculosis* H37Rv and found that the Co(II) complex becomes equipotent to the standard drug Isoniazid. *C. Leelavathy et al*[27] have reported the synthesis of Co(II), Ni(II), Cu(II) and Zn(II) complexes **(20)** of Schiff base derived from furfurylidene-4-aminoantipyrine and 2-aminobenzothiazole. The in vitro biological screening of the ligand and its complexes were tested against bacterial species indicate that activity increases on chelation. The DNA binding and cleavage activity of the ligand and their complexes were evaluated. Super oxide dismutase (SOD) activities of the ligand and its complexes have also been measured.



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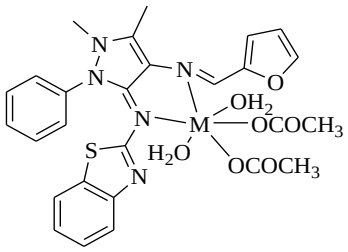

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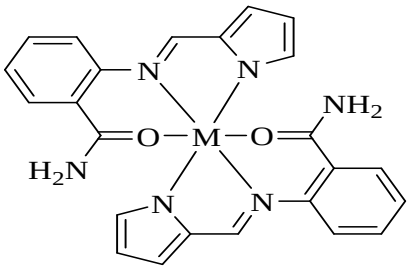
A series of two biologically active Schiff base ligands, synthesized from 2-aminobenzamide by reacting with pyrrol-2-carboxaldehyde and furan-2-carboxaldehyde, and their Co(II), Ni(II) and Cu(II) complexes have been reported by *P. Tyagi et al*.[28] All the compounds were screened for their antimicrobial activity which reveals that metal(II) complexes shows significant activities than the ligands against different bacterial and fungal strains. *M. Grazul et al*[29] have reported the synthesis of Co(II) and Pd(II) complexes of 5-amino-8-methyl-4H-benzopyran-4-one and evaluated as potential anticancer compounds against several cancer cell lines.



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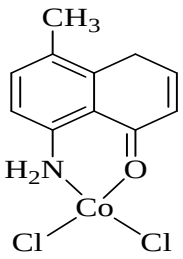
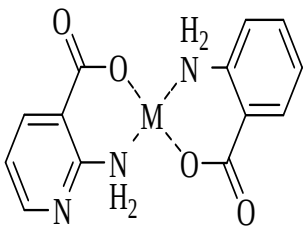


22

M. Nawaz et al[30] have synthesized 2-aminonicotinic acid (2-ANA) complexes **(23)** with Co(II), Fe(III), Ni(II), Mn(II), Zn(II), Ag(I), Cr(III), Cd(II) and Cu(II) metals. The metal complexes showed varied antibacterial, fungicidal and nematicidal activities. The activity data indicate that the silver and zinc complexes showed highest activity against *Bacillus subtilis* and *Bacillus licheniformis* respectively. *Fusarium oxysporum* was highly vulnerable to nickel and copper complexes while *Macrophomina phaseolina* was totally inert to the complexes. In addition, the silver and cadmium complexes were effective against the root-knot nematode *Meloidogyne javanica*. *A.A. El-Sherif et al*[31] have reported the synthesis of a new hydrazone ligand (2-((2-phthalazin-1-yl)hydrazono)methyl)phenol), by condensation of hydralazine (1-Hydralazinophthalazine) with salicylaldehyde, and its Ni(II), Co(II) and Cu(II) complexes **(24)** and evaluated for their potent antimicrobial activities against the selected bacteria and fungi.



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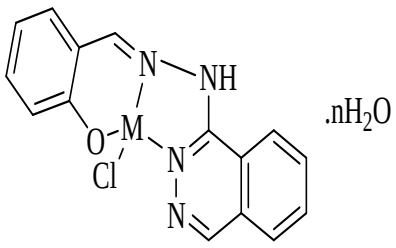

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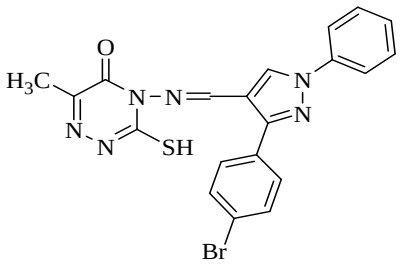
K. Singh et al[32] have synthesized a new series of Co(II), Ni(II), Cu(II) and Zn(II) complexes with bidentate ligand **(25)** derived by condensation of 4-amino-3-mercapto-6-methyl-5-oxo-1,2,4-triazine with 3-(p-bromophenyl)-1-phenyl-1H-pyrazolecarboxaldehyde. Schiff base and its metal complexes were screened for *in vitro* antimicrobial activity and it was observed that metal complexes show enhanced biological activity as compared to ligand or metal salts. In addition, Zn(II) complexes show enhanced biological activity against most of the microbial strains as compared to ligand and other metal complexes. *K.H.K. Naik et al*[33] have reported the synthesis and characterization of the transition metal complexes **(26)** containing tri-dentate NSN donor ligands i.e., 5-

((1(aminomethyl)cyclohexyl) methyl)-1,3,4-thiadiazol-2-amine and 5-(2-aminophenyl)-1,3,4-thiadiazol-2-amine and evaluated for effective anti-inflammatory, analgesic and DNA binding activities. All the tested compounds exhibited considerable analgesic activity, where the Mn(II) and Co(II) complexes of ligand 4 is equipotent with Diclofenac sodium.



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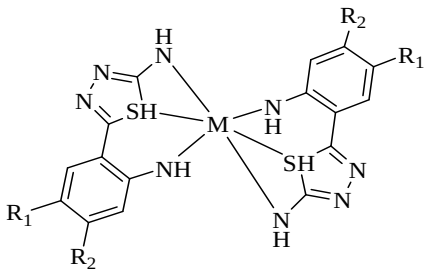
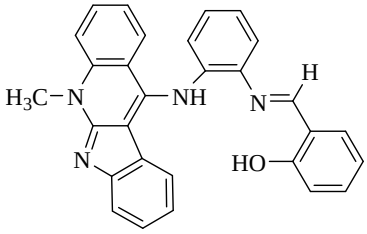


26

S.M. Emam et al[34] have synthesized three new Shiff base ligands (**27)** from aminoneocryptolepine and their Co(II), Ni(II), Cu(II), and Pd(II) complexes. Furthermore, the ligands and their complexes were screened for their anticancer activity against colorectal adenocarcinoma (HT-29) cells and found Co(II) complexes exhibited higher anticancer activity when compared to the ligands. *P. Krishnamoorthy et al*[35] have synthesized and characterized the divalent Co, Ni and Cu hydrazone complexes containing N'-(phenyl(pyridine-2-yl)methylidene) benzohydrazide ligand (**28)**. Interactions of these complexes with DNA revealed an intercalative mode of binding between them. Further, assay on the cytotoxicity of the complexes against HeLa tumor cells and NIH-3T3 normal cells revealed that the complexes are toxic only against tumor cells but not to normal cells, with enhanced activities with copper ion.



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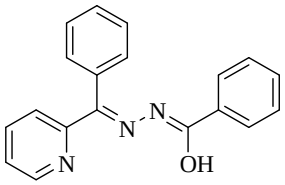

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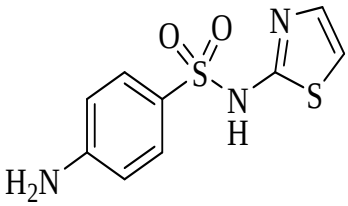
F. Ozturk et al[36] have described the synthesis, spectroscopic and electrochemical characterization of Cu(II)-sulfathiazole complexes **(29)**. Further, Antibacterial evaluation of the Cu(II)-sulfathiazole against bacterial and fungal strains, complex showed very strong antibacterial activity with MIC values ranging from 1 to 4 µg/mL. *V. Kumar et al*[37] have described first time synthesis of silver metal complex of phenothiazine **(30)**, which displayed superior antimicrobial activity against various strains, good antioxidant activity, and medium binding with BSA protein.



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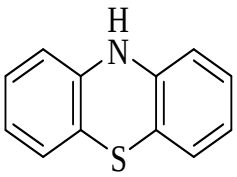

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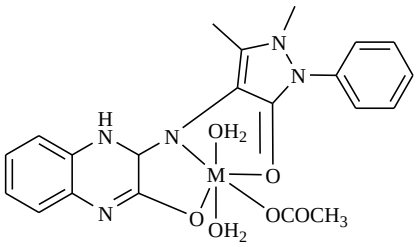
C.J. Dhanaraj and J. Johnson[38] have synthesized novel Co(II), Ni(II), Cu(II) and Zn(II) complexes **(31)** of Schiff base derived from quinoxaline-2,3-(1,4H)-dione and 4-aminoantipyrine. The *in vitro* biological screening of ligand and its metal complexes were tested against bacterial species namely *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* and fungal species as *Aspergillus niger*, *Aspergillus flavus* and *Candida albicans*. Additionally, the DNA cleavage activity was also studied. *S. Daravath et al*[39] have synthesized two novel Schiff bases, 2-benzo[d]thiazol-6-ylimino)methyl)-4,6-dichlorophenol and 1-benzo[d]thiazol-6-ylimino)methyl)-6-bromo-4-chlorophenol, and their Cu(II), Co(II) and Ni(II) complexes **(32)**. DNA cleavage experiments of metal(II) complexes showed that the Cu(II) complexes cleaved

DNA more effectively compared to Co(II), Ni(II) complexes. Besides, the ligands and their metal complexes were screened for antimicrobial activity and the metal complexes were found to be more potent than free ligands.



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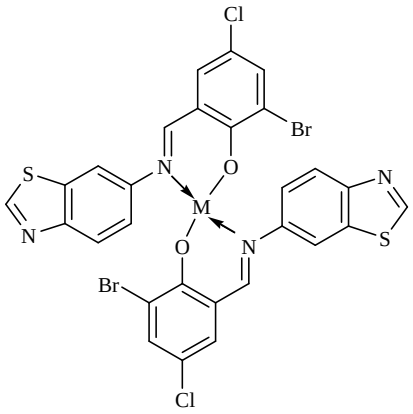
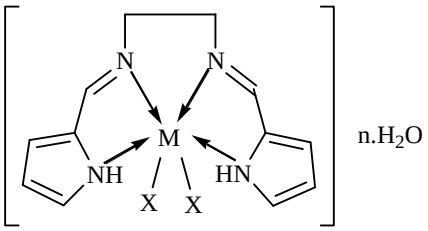


32

The new symmetrical Schiff base N,N-bis(pyrrole-2-carbaldehyde)ethylenediamine and its Mn(II), Co(II), Ni(II) and Cu(II) complexes **(33)** were synthesized and characterized by *B.K. Singh et al*.[40] Moreover, the bio-efficacy of the ligand and its complexes has been tested against the growth of bacteria *in vitro* to evaluate their anti-microbial potential. *S. Chandra et al*[41] have synthesized a novel Schiff's base ligand, benzil bis(5-amino-1,3,4-thiadiazole-2-thiol) and its Ni(II), and Cu(II) complexes **(34)** and screened for their promising antibacterial and antifungal activities.



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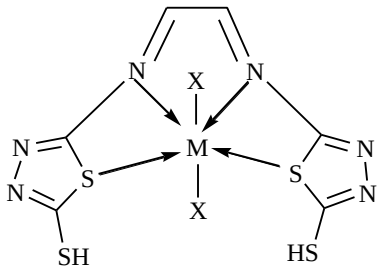
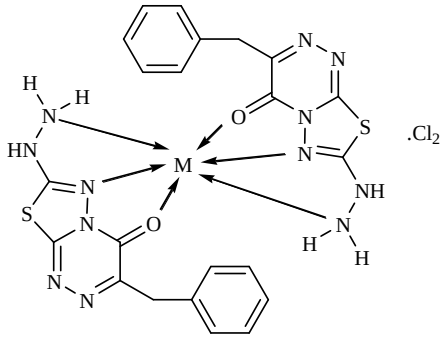


34

G.G. Mohamed et al[42] have reported the coordination behaviour of the triazine ligand with NNO donation sites, prepared from 3-benzyl-7-hydrazinyl-4*H*-[1,3,4]thiadiazolo[2,3c][1,2,4]triazin-4-one, towards transition metals. Further, the synthesized ligand and its metal complexes **(35)** were examined against the desert locust *Schistocerca gregaria* and its adult longevities. The activity data showed that the complexes are found to play an important role in regulating activity oviposition rhythm of locust *Schistocerca gregaria*. *M.P. Sathisha et al*[43] have described the synthesis, structure, physico-chemical investigation and biological studies of Co(II), Ni(II) and Cu(II) complexes **(36)** of bis(3-acetylcoumarin)thiocarbohydrazone ligands. The metal complexes examined have shown promising cytotoxic activity. In addition, the antimicrobial screening shows the promising results against both bacterial and fungal strains.



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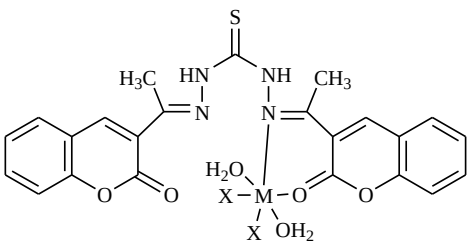
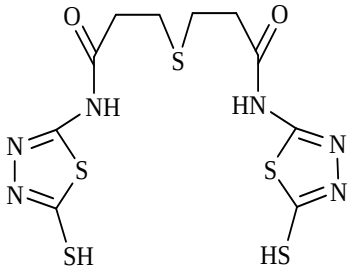


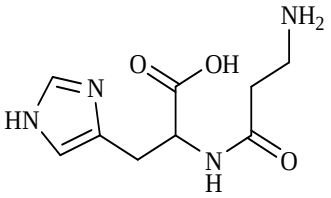
36

S. Chandra et al[44] have reported the synthesis and characterization of nickel(II), and copper(II) Complexes of pantadentate ligand 3,3'-thiodipropionicacid-bis(5-amino-1,3,4-thiadiazole-2-thiol) **(37)**. Additionally, *in vitro* fungicidal study of ligand and its complexes was examined against fungi Candida albicans, Candida parapsilosis, Candidia krusei, and Candida tropicalis.



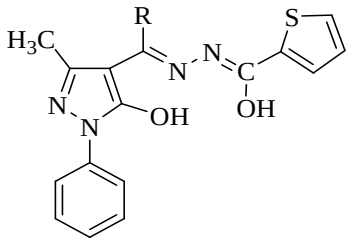
37

E.M. Moustafa et al[45] have described the calculated binding modes and binding energies of protonated carnosine **(38)** and canosine metal complexes and some common Pt-based anti-cancer drugs both in the gas phase and in solution.



38

Two new Mn complexes based on 4-acyl pyrazolone derivatives **(39)** have been prepared, structurally characterized and biologically evaluated by *Y. Li et al*.[46] The inhibitory effects of the complexes on the cell population growth of the human esophageal cancer Eca-109 cells and the cervical cancer HeLa cells were observed significantly. Furthermore, the complex 1 inhibited the growth of HeLa cells through inducing the apoptosis and arresting cell cycle at S phase. The data results suggested that both complexes have DNA and protein-binding capacity and antitumor activity. Triazole **(40)** appended mixed ligand complexes of Cu(II), Co(II), Ni(II) and Zn(II) have been synthesized by *P.P. Utthra et al*.[47] The complexes were found higher DNA damaging efficacy compared to the ligand. Furthermore, the complexes possess excellent antimicrobial activity against bacterial and fungal strains than the ligand.



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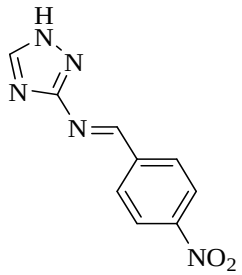
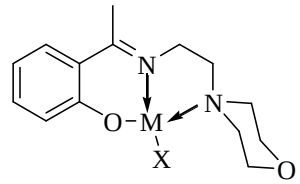


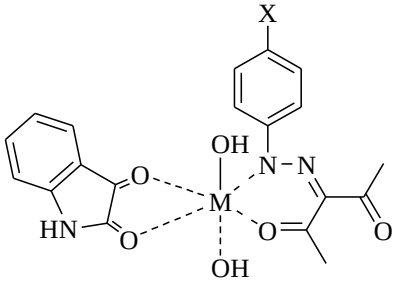
40

A series of the Schiff bases complexes **(41)** derived from marpholine were reported for their moderate cytotoxicity mediated on MCF-7 breast cancer cell line and found selective to some extent when compared with the WRL68 normal liver cell line.[48] *S.A. Osman et al*[49] have synthesized Ni(II), Co(II) and Mn(II) complexes **(42)** of 3-(2-arylhydrazono)acetylacetone and isatin. Additionally, the ligands and their metal complexes were tested for cytotoxicity against different human cancer cell lines using the sulforhodamine B assay where most of the mixed ligand metal complexes have high cytotoxicity than the standard drug.



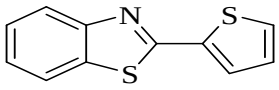
M = Cu, Mn, Ni or Zn

41



42

Synthesis, characterization, DFT simulation and biological assays of two new metal complexes of 2-(2-thienyl) benzothiazole **(43)** have been reported by *G.A. Pereira et al*.[50] The activity data showed Silver (I) complex become more effective against M. tuberculosis than the commercial drug silver sulfadiazine (SSD). The gold complex also showed a good antitubercular activity while free BTT shows very low activity against M. tuberculosis. *L. Zhang et al*[51] have reported four metal complexes based on quinoline carboxylate ligand **(44)** from 2-(pyridin-4-yl)quinoline-4-carboxylic acid. All the complexes were screened for their antibacterial activity. The bioassay result data indicate that Co(II) and Cd(II) complexes exhibit antibacterial activity against gram-positive bacteria *B. subtilis* and *S. aureus*, and Ag(I) complex exhibits antibacterial activity against *P. aeruginosa*.



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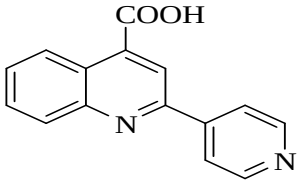
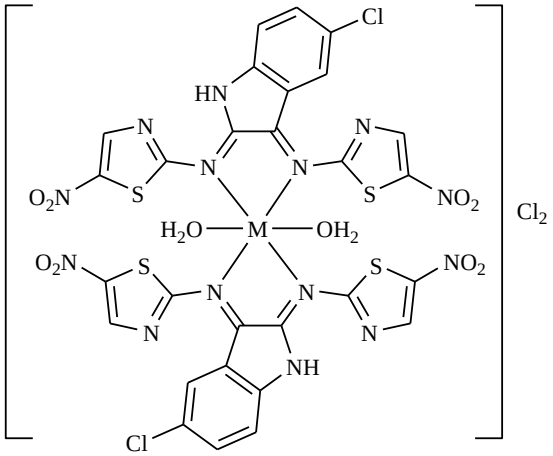


44

Novel bioactive 5-chloro isatin based Schiff base ligands, prepared from 2-amino 5-nitrobenzothiazole and 2-amino 5-nitrothiazole, and their metal complexes **(45)** have been synthesized by *M. Shakir et al*.[52] In addition, *in vitro* antibacterial and scavenging activies of the synthesized complexes were studied. *In vitro* cytotoxicity of ligands and its metal complexes was also carried on MCF7, HeLa and HepG2 cell lines along with normal cells. The antiproliferative effect revealed that metal complexes exhibit superior activity compared to free ligands. A series of VO(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes **(46)** have been synthesized from 3/2-pyrazolone azo Schiff base ligand by *C. Anitha et al*.[54] The interaction of synthesized complexes with CT-DNA showed that Co(II) and Cu(II) complexes cleave DNA in the presence of H_2O_2. Additionally, the antibacterial and antifungal activities showed that the metal complexes have a promising activity comparable with the parent Schiff base ligand against bacterial and fungal strains.



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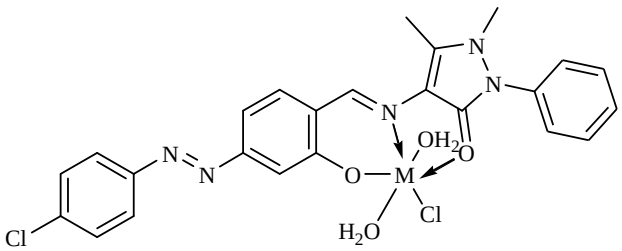
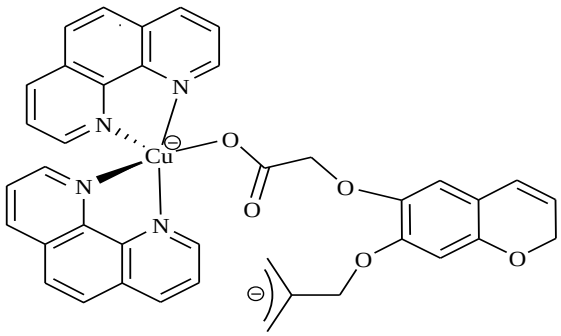


M = Co(II), Ni(II), Cu(II) and Zn(II)

46

B. Thati et al[53] have investigated the potential *in vitro* anti-proliferative properties of coumarin-dioxy-acetic acid ligand and its copper complex **(47)**, copper-coumarin-dioxyacetic acetate-phenathroline using four human-derived model cell lines, two neoplastic and two non-neoplastic. The activity data obtained show that the complex alters the proliferation of both human neoplastic renal (A-498) and hepatic (Hep-G2) cells. *W.H. Mahmoud et al*[55] have reported the coordination behavior of a series of transition metal ions with a mono negative tridentate guaifenesin ligand and 1,10-phenanthroline. All the complexes **(48)** along with guaifenesin ligand were screened for their antibacterial and antifungal activity where the activity data show that the metal complexes have more potent than the parent GFS ligand. The complexes were also screened for their *in vitro* anticancer activity against the Breast cell line (MFC7).



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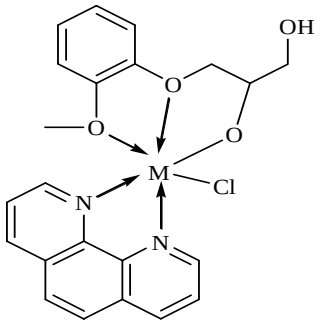
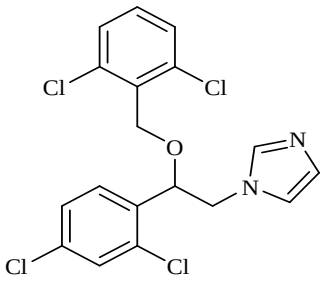


M = Mn(II), Zn(II) and Cu(II)

48

Keeping in view of growing demand for new metal-based complexes with biologically significant molecules in medicine and technology, three new Cu(II) coordination compounds with antifungal agent isoconazole **(49)** namely two mononuclear complexes and one dimensional coordination polymer were synthesized and characterized by *G.M. Dulcevscaia et al*.[56] The biosynthetic ability of *Aspergillus niger* CNMN FD 10 in the presence of Cu(II) complexes as well as the antifungal drug isoconazole showed that both complex and isoconazole nitrate displayed pronounced inhibitory effect on the enzymatic activity. *M.X. Li et al*[57] have reported the synthesis and characterization of two NNS tridentate Schiff base ligands 2-benzoylpyridine S-methyl/phenyl dithiocarbazate **(50)** and their Cu(II) and Zn(II) metal complexes. MTT assay was carried out to evaluate cytoxicity in K562 leukaemia cell line and QSG7701 cell line. The activity data emphasized that Zn(II) and Cu(II) complex effectively inhibit K562 leukaemia cell line at concentrations more than 61-fold and 8-fold respectively lower than parent ligand.



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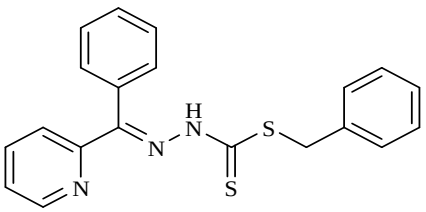
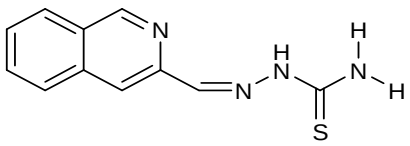


50

Thiosemicarbazone **(51)** of napthaldehyde, quinoline-2-carbaldehyde and salicylaldehyde, and their copper(II) complexes have been reported *Saswati et al*.[58] All the complexes were investigated for their DNA-binding and cleavage activity. Among the complexes, quinoline bearing Cu(II) complex shows the highest DNA cleavage activity against pUC19 DNA. In addition, the *in vitro* antiproliferative activity of all the complexes was examined against the HeLa cell line. Where the greater potency of quinoline bearing Cu(II) complex was observed may be correlated with its aqueous solubility and the presence of the quinonoidal group coordinated to the metal. M. Aljahdali[58] reported the synthesis and characterization of a series of four 2-aminomethylbenzimidazole-glycine based ternary complexes **(52)** of Cu(II), Zn(II), Ni(II) and Cd(II). The synthesized chelates were screened for their antifungal and antibacterial activities. Where the copper(II) complex showed the most promising potent broad spectrum antimicrobial compound among the synthesized complexes. Additionally, the cytotoxic activity of the complexes against colon (HCT116) and larynx (HEP2) cancer cells were evaluated.



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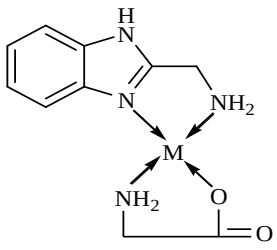
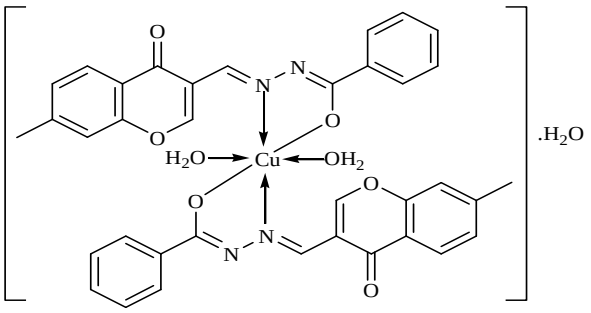


52

J.E. Philip et al[60] have reported the synthesis and characterization of two chromone hydrazone ligands and their transition metals complexes with Ni(II), Cu(II), and Zn(II) metals **(53)**. The DNA binding properties of the complexes were studied where these complexes bind to DNA by an intercalative mode. The ligand and its complexes were also screened for the enzyme inhibition activity against α-amylase and α-glucosidase. Besides, ligand and its transition metal complexes have shown analogous antidiabetic activity with a standard drug acarbose. A.M.A. Adam[61] have investigated the metal complexation **(54)** of 8-chlorotheophylline with Cr(III), Mn(II), Co(II), Ni(II), and Cu(II) metals as 8-chlorotheophylline exhibits high stimulant action. The effect of chelation on the bioactivity of 8-chlorotheophylline were studied. The activity data showed that 8-chlorotheophylline possesses very low inhibitory activity against several bacterial and fungal strains. Though, the potency of Cr(III)-complex go beyond that of the standard drug Ciprofloxacin against all of the tested bacterial strains.



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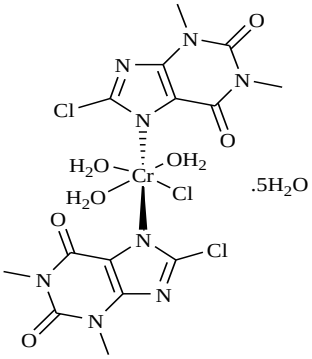
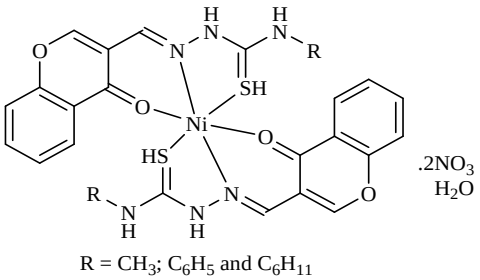


54

S. Selvamurugan et al[62] have reported the synthesis and characterization of the new nickel(II) complexes **(55)** containing 4-chromone N(4)-substituted thiosemicarbazone ligands. The newly prepared complexes were studied for DNA/protein interaction where the activity data showed that the complexes are capable of binding with DNA via intercalative mode while protein binding studies revealed that the new complexes also have the tendency to bind strongly with bovine serum albumin. Further, the complexes showed superior anticancer activity against MCF-7 cancer cell line. *P. Sathyadevi et al*[63] have derived three new transition metal complexes of *N*'-[phenyl(pyridin-2-yl)methylidene]furan-2-carbohydrazide. Furthermore, the complexes were subjected for their DNA cleavage ability and show the potential nuclease activity to cleave the supercoiled form into the nicked form. *In vitro* assay on the antioxidant activity of the complexes and hydrazone ligand showed that the Cu(II) complex **(56)** exhibited superior activity than the other complexes in terms of the ABTS radical cation, lipid peroxidation and NO radical scavenging assays.



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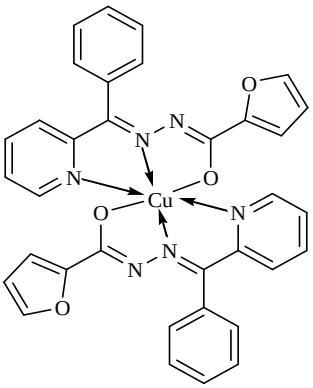
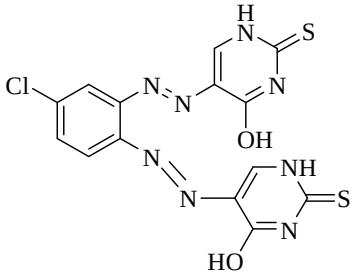


56

S. Al-Ashqer et al[64] have prepared and investigated γ-irradiation effect of a series of Ni(II), Pt(IV) and UO_2(II) complexes of thiouracil ligand **(57)**. Additionally, all the complexes were studied for toxicity. The activity data revealed that the complexes show a toxic effect towards Gram positive bacteria and a resistant behavior with Gram negative bacteria. M. Hanif and Z.H. Chohan[65] have synthesized a new series of three biologically active triazole derived Schiff base ligands, from 3-amino-1*H*-1,2,4-triazole, and their Co(II), Ni(II), Cu(II) and Zn(II) complexes **(58)**. All the synthesized compounds were screened for their *in vitro* antibacterial and antifungal activities. Furthermore, the compounds were carried out to investigate the *in vitro* cytotoxic effect of these compounds.



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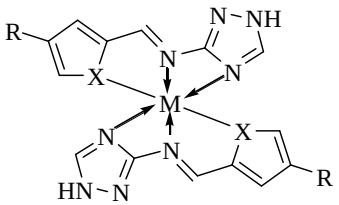

X = N R = H, X = S R= Br
M = Co(II), Ni(II), Cu(II) and Zn(II)

58

The bioactive Ni(II), Co(II), Cu(II) and Zn(II) complexes of pyrazoline derivatives have been reported for their antimycobacterial activity.[66] Further, the Ru(η^6-*p*-cymene) Complexes of indole thiosemicarbazole[67] and Fe(III), Co(II) and Ni(II) complexes of 3-[(*E*)-(4*H*-1,2, 4-triazol-4-ylimino)methyl]quinoline-2-thiol[68] were exclusively studied for their in vitro anticancer activity.

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