

The Role Of Schiff Bases In The Antibacterial Activities And Medical Applications

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Abstract—Schiff bases are condensation of primary amines with carbonyl groups. Because of carbon nitrogen interaction Schiff bases show high antimicrobial properties. In this review we have discussed in different synthesis and applications of azomethines. In different ways we proved that can be produce very easy conditions. Investigations of many scientific works we concluded two wings antibacterial and medical uses of azomethines. We have also discussed our scientific research in the side of Schiff bases and usage of them multifunctional compounds. We concluded that our compounds maintain their antimicrobial properties in a very low concentration (0,25% concentration) and long period of time (6 months)

Keywords—Schiff bases, metal complexes, antibacterial activity, azomethines, antioxidant properties.

Introduction.

Schiff Bases are condensation of primary amines with carbonyl compounds [1] and they were first reported by Schiff in 1864 [2]. The common structural feature of these compounds is the azomethine group with a general formula $RHC=N-R_1$, where R and R_1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines. Several studies have shown that the presence of a lone pair of electrons in an sp^2 hybridized orbital of nitrogen atom of the azomethine is group of considerable chemical and biological importance. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group. Schiff bases are generally excellent chelating agents, especially when a functional group like -OH or -SH is present close to the azomethine group so as to form a five or six membered ring with the metal ion versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable[3]. Nowadays, the research field dealing with Schiff base coordination chemistry has expanded enormously. The importance of Schiff base complexes for bioinorganic chemistry, catalysis and material science, separation and encapsulation processes, and formation of compounds with unusual properties and structures has been recognized and reviewed[4].

Schiff bases resulted from aromatic aldehydes ortho-substituted with a hydroxyl group have initially aroused the researchers interest because of their ability to act as bidentate ligands for transitional metal ions[5]. Later, in studies concerning quantitative structure antitumor activity relationship of a series of Schiff bases derived from variously substituted aromatic amines and aldehydes, it has been shown that azomethines from salicylaldehydes gave the best correlation. Schiff bases of salicylaldehydes have also been reported as plant growth regulators and antimicrobial or antimycotic activity. Schiff bases also show some analytical applications. Schiff Bases are characterized by the $-N=CH$ (imine) which imports in elucidating the mechanism of transamination and rasemination reaction in biological system. Schiff bases are active against a wide range of organisms for example: *Candida Albicans*, *Escherichia coli*, *Staphylococcus aureus*, *Bacillus polymyxa*, *Trychophyton gypseum*, *Mycobacteria*, *Erysiphe gramminis* and *Plasmopora viticola*[6]. A large number of different Schiff base ligands have been used as cation carriers in potentiometric sensors as they have shown excellent selectivity, sensitivity, and stability for specific metal ions such as Ag(2), Al(3), Co(2), Cu(2), Gd(3), Hg(2), Ni(2), Pb(2), Y(3), and Zn(2)[7]. Schiff bases have been studied for their important properties in catalysis. They show catalytic activity in hydrogenation of olefins. They find applications in biomimetic catalytic reactions[8]. An interesting application of Schiff bases is their use as an effective corrosion inhibitor, which is based on their ability to spontaneously form a mono layer on the surface to be protected.

Many commercial inhibitors include aldehydes or amines, but presumably due to the C=N bond the Schiff bases function more efficiently in many cases. The principal interaction between the inhibitor and the metal surface is chemisorptions. In such cases the metal acts as an electrophile and the inhibitor acts as a Lewis base. Nucleophilic centers, such as oxygen and nitrogen atoms, of the protective compound have free electron pairs which are readily available for sharing. Together with the atoms of the benzene rings they create multiple absorption sites for the inhibitor thus enabling stable monolayer formation[9]. Imines also have biological importance. An imine linkage between the chemistry of vision. Their metal complexes have been widely studied because they have anticancer and herbicidal

applications. They serve as models for biologically important species[10].

Report of synthesis and applications

Three new series of biologically active amino substituted Schiff bases with general formula, $R_1N=CHR_2$. Here $R_1=2$ -amino-benzothiazole, 4-amino-salicylic acid and aminophenol. $R_2=4$ -chloro-benzaldehyde, 2-chloro-benzaldehyde, salicylaldehyde, vanillin and benzaldehyde were synthesized by the reaction of three different amino substituted compounds were characterized by different physico-chemical techniques like, melting point, elemental analysis, multinuclear NMR($^1H, ^{13}C$). The free ligands and their metal complexes have been screened for their in vitro biological activities against bacteria, fungi and yeast. The metal complexes show more potent activities compared with Schiff base ligands. These compounds exhibited significant activity against all the tested microorganisms [11].

The scientist of Damascus University have been synthesized 1,4-Bis(3-aminopropyl)-piperazine was condensed with various aromatic aldehyde in ethanol in the presence of acetic acid as catalyst to yield the Schiff base. These Schiff bases on treatment with phthalic anhydride gave substituted oxazepine. In this work the inhibiting action of Schiff bases and their derivative on the corrosion steel in 1M H_2SO_4 solution has been investigated. The electro chemical techniques such as polarization measurements were used in this study. Differences in behavior of inhibitors were explained based on structural properties of investigated inhibitors [12].

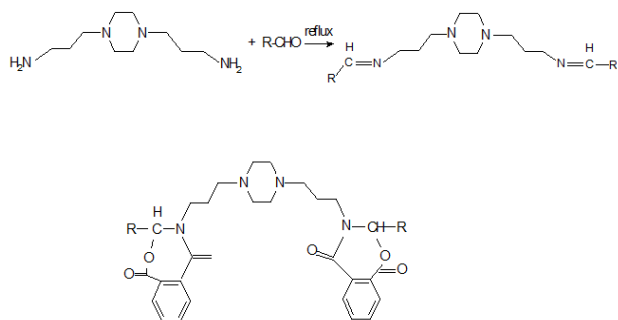


Fig1. oxazepine

It is evident from literature that isatin derivatives are known to be associated with broad spectrum of biological activity. In view of these facts and a continuation of their work in the laboratory Indian scientists prompted as to synthesize some new 3-[(5-benzylidene-2-phenyl)-3,5-dihydro-4H-imidazol-4-one-3-(4-benzoylhydrazono)]-indole-2-ones. All the synthesized compounds were screened for their in vitro antibacterial and antifungal activity. As many as new fourteen compounds were synthesized by adopting similar above procedure and then characterized by their physical, analytical and spectral data. The details of some of the representative compounds are given in the experimental section. Their physical and elemental analysis data are

presented. All the synthesized compounds were tested for in vitro antimicrobial activity by the disk diffusion technique. The tested compounds exhibited mild to moderate antibacterial activity against all strains of bacteria. The compounds tested against *S.aureus*, showed highest activity. It has also been observed that compounds showed activity against *B subtilis*. All the synthesized compounds were tested for in vitro antimicrobial activity by the disk diffusion technique. The antimicrobial study revealed that substitution in the 5th position of isatin with chlorine, bromine or fluorine produce more active compounds in a series[13].

Many compounds carrying 3(2H)-pyridazinone and 1(2H)-phthalazinone rings are known to have different biological activities such as antiplatelet, antihypertensive, analgesic, and anti-inflammatory actions. However, some compounds bearing 3(2H)-pyridazinone or 1(2H)-phthalazinone ring have been reported to have antimicrobial activity. In addition, some benzenesulfonylhydrazide derivatives have been reported to have antibacterial activity. On the basis of these findings the scientist of Gazi University have been synthesized some 3(2H)-pyridazinone and 1(2H)-phthalazinone derivatives. The synthesized compounds were evaluated for their antibacterial activity against various gram-positive and gram-negative strains of bacteria and their clinical isolates and for their antibacterial activity against *M.tuberculosis* H37Rv. [14]

The compounds possessing higher activities. This has led to concentrate deep research on this class of compounds and their metal complexes. Similarly, the presence of hetero-atoms in the Schiff bases enhances activity. On the basis of Indian scientists work to understand the role of fine electronic variations on molecular activity and the effect of substituent location in salicylidene-2-aminopyridine Schiff bases on the absorption spectra in inorganic solvents of changeable polarities and their antibacterial activity against some common pathogens against some common pathogens namely *Staphylococcus aureus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Escherichia coli*. On this bases scientists have been synthesized (1) N-(2-hydroxybenzylidene) pyridine-2-amine, (2) N-(5-nitro-2-hydroxybenzylidene) pyridine-2-amine, (3) N-(5-bromo-2-hydroxybenzylidene) pyridine-2-amine, (4) N-(5-methoxy-2-hydroxybenzylidene) pyridine-2-amine are prepared from 2-aminopyridine and substituted benzaldehydes. The synthesized compounds are characterized, (4) N-(5-methoxy-2-hydroxybenzylidene) pyridine-2-amine are prepared from 2-aminopyridine and substituted benzaldehydes. The growth prevention capability was affected by the solvent and substitute group on the salicylidene part. The compounds have the ability to preventing metabolic growth of *S.aureus* and *E.coli* to different extent. The antimicrobial activity of the compounds depends on the nature of substituted present in the nature of

present on the aldehyde. The importance of this lies within the potential use of the compounds as narrow spectrum antibiotics in treatment of some common diseases[15].

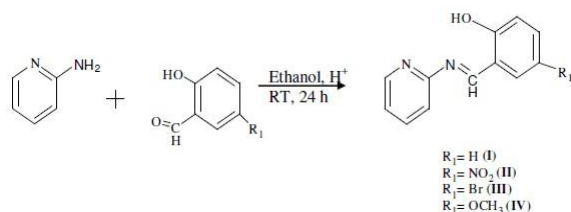
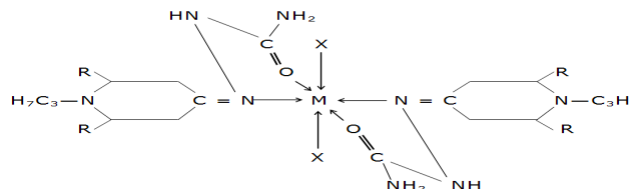


Fig2 (4)*N*-(5-methoxy-2-hydroxybenzylidene) pyridin-2-amine

Pyrazoles with various functional groups at position-4 such as cyano or oxime, aldehyde or carboxylate have been known to show good antimicrobial properties. In view of these and in continue of our research on biologically active molecules we hereby report the synthesis of some new Schiff bases bearing triazole and pyrazole and their antibacterial studies. In the present study a series of new Schiff bases were synthesized. All the synthesized compounds were characterized by IR, HNMR, mass spectral and elemental analyses. Newly synthesized compounds were screened for their antibacterial activity. The results revealed that, compounds have exhibited significant biological activity against the tested microorganisms[16].

Wide varieties of geometries and reactivity of semicarbazone metal complexes have been reported to possess several biocidal activity of semicarbazone have been subject of investigation in recent years. The biological activity is related to their interaction with several metal ions Schiff bases ligand and their metal complexes play an important application in the area of analytical chemistry, polymer sciences, food and dyes industry, agriculture biological sciences as antimicrobial agents, medical sciences as anticancer and metal corrosion inhibition agents. In view of the growing interest in the biocidal importance of Schiff and their metal complexes and in continuation of our earlier recent work in this field we now report, the synthesis, characterization and antibacterial activity of Cu(2), Co(2), Ni(2) complexes with bidentate Schiff base 1-propyl-2-6-diphenylpiperidone semicarbazone. On the bases of this work a series of metal complexes derivatives of 1-propyl-2-6-diphenyl piperidone semicarbazone(PDRS) with metal ions Cu(2),Co(2), Ni(2) have been synthesized. The ligand and metal complexes obtained are characterized quantitatively by using, molar mass, elemental analysis, infrared spectra electronic spectra, magnetic susceptibility and conductivity measurements. It has been observed that the ligand PDRS coordinate to the metal ion in a bidentate manner through azomethine nitrogen and oxygen atom of semicarbazone moiety. The remaining coordinatipon centers are satisfied by anions such as X=Cl, Br, I. Electronic spectral

measurement proposed the general composition of the complexes $[M(\text{PDRS})_2\text{X}_2]$ where $M=\text{Cu}(2),\text{X}=\text{Cl}$ and Br, I. The complexes of Co(2),Ni(2) were proposed octahedral geometries whereas distorted octahedral geometry reported for Cu(2) complexes. The preliminary in vitro antibacterial screening activity revealed that complexes showed better inhibition against tested bacterial strains and higher compared to parent ligand [17].



The synthesis of unsymmetrical Schiff base has attracted more interest. Although unsymmetrical ligands can clearly offer many advantages over their symmetrical counter parts in the elucidation of the composition and geometry metal ion binding sites in metalloproteins, and in the development leading to the duplication of enzymatic efficiency and selectivity of natural systems with synthetic materials, the difficulty of preparation of such ligands has hampered progress because simple condensation methodology with three components is no longer applied. In this paper we report the syntheses, structural characterization and biological activities of Cu(2),Zn(2),Ni(2), and Mn(2) complexes of the new Schiff base ligand synthesized from 2-hydroxy-1-naphtaldehyde and 5-amino-1-naphtol. The new complexes were investigated spectropically and biological activity[18].

Compounds containing the sulphonamide group have long been used as drugs for diseases Sulpha drugs with aldehydes, ketons or their derivatives are biologically very active, besides having good complexing ability, their activity has also been shown to increase on complexation with metal ions. The new coordination complexes of Co(2),Ni(2), and Cu (2) have been synthesized from Schiff base derived from sulfapyridine and 2-hydroxynaphthaldehyde. The nature of bonding and the structural features of the Schiff base and its complexes have been deduced from elemental analysis, molar conductance, magnetic susceptibility measurements, Cyclic Voltammetry. These Schiff base and its metal complexes exhibited enhances antimicrobial activity compare to uncomplexed Schiff base [19].

The chemistry of 1,2,4-triazole and its fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. 1,2,4- triazole moieties have been incorporated into variety of therapeutically interesting drug candidates including antiviral (ribavarin), antimigraine(rizatriptan), antifungal(flucanazole) antianxiety compounds(alprazolam). The pharmacological

importance of heterocycles derived from 1,2,4-triazole paved the way towards active research in a triazole chemistry. In view of these and in continuation of our research on biologically active molecules we hereby report the synthesis of some new Schiff bases bearing triazole and pyrazole moieties and their antibacterial studies[20].

Some Schiff bases were tested for fungicidal activity, which is related to their chemical structure, there metal complexes are important in biochemical process. For example, the transamination reactions are catalyzed by metals ions through the formation of intermediate Schiff bases containing vitamin B6. In the area of bioinorganic chemistry interest in Schiff base complexes has centered on the role of such complexes in providing synthetic models for the metal containing sites in metalloproteins and enzymes. Schiff base ligands are potential anticancer drugs and the anticancer activity of these metal complexes are enhanced in comparison to their free ligands.

3,4-dihydroxybenzaldehyde, (Protocatechuaaldehyde,PCA) derivatives were evaluated and showed inhibition for bacteria growth, antioxidant, antitumor, anticorrosion and reagent in simple and highly sensitive analyses of Cr(4),(5)[21].

Some substituted aminothiazole derivatives are used as antioxidant additives to hydrocarbon fuels, minerals and synthetic lubricating oils, solid paraffin, polyolefins and vegetable fats. Sym triazine derivatives containing substituents with 2-aminothiazole fragments are effective anticorrosive, antiwear and antiscuff additives to lubricating oils. In continuation of our work 7-14 on the metal complexes of Schiff bases, we report here the study of Schiff base metal complexes of Mn(II), Fe(II), Co(II), Ni(II) and Cu(II) derived from 2-amino-4-phenylthiazole and substituted 4-acetyl-1-phenyl-3-methyl-2-pyrazolin-5-one. Preparation, characterization and antibacterial activity of above metal complexes with Schiff bases Ligand-L and Ligand-L1 are also reported here.[22].

The chemistry of metal complexes containing salen-type base ligands derived from condensation of aldehyde and amines is of enduring significance. Since they have common features with metalloporphyrins with respect to their electronic structure and catalytic activities that mimic enzymatic oxidation In this paper, we report the synthesis, structural characterization and biological activities of Cu(II), Zn(II), Ni(II) and Mn(II) complexes of the new Schiff base ligand synthesised from 2-hydroxy-1-naphthaldehyde and 5-amino-1-naphthol. The new complexes were investigated by IR, electronic spectra, cyclic voltammetry, conductivity measurement, EPR studies and biological activity[23].

Schiff bases and Mannich bases of isatin are known to possess a wide range of pharmacological properties including antibacterial, anticonvulsant, anti-HIV, antifungal and antiviral activity. Bis-Schiff

bases are characterized by their capacity to completely co-ordinate a metal ion, forming chelate rings. The Schiff bases of isatin have also been used as ligands for complexation of metals such as copper II. These complexes catalyzed the oxidation of carbohydrates. Bis-Schiff bases can act as inhibitors of human α -thrombin. Recently it has been reported that a bis-imine of isatin has antimicrobial properties and affects cell viability. Here we report the synthesis and characterization of new bis-Schiff bases of isatin, benzylisatin and 5-fluoroisatin, which could be considered as potential biologically active compounds. In the present study we have reviewed the synthesis and different biological activities of some Schiff bases of imidazo-1, 3, 4-thiadiazole derivatives. The Schiff base is functional group that contains a carbon- nitrogen double bond with nitrogen atom connected to an aryl or alkyl group but not hydrogen. Schiff bases can be synthesized from a substituted aromatic amines and a carbonyl compound by nucleophilic addition forming a hemiaminal followed by dehydration to generate an imine. The synthesis part starts with the condensation of 1, 3- benzodioxole-5-carboxylic acid and thiosemicarbazide in the presence of POCl₃ under reflux to form thiadiazole derivative, various thiadiazoles are further condensed with phenacyl bromide to obtain imidazo thiadiazole derivatives which on treatment with DMF and POCl₃ gives 5-formyl derivatives. The formyl functional group has been utilized to synthesize corresponding Schiff bases. The substituted derivative show moderate biological activity. Further the prepared Schiff bases have been subjected to antimicrobial property. The derivative has shown moderate to good activity when compared with standard antibiotic ampicillin. [24].

1, 3, 4 -Thiadiazole are diversified biocidal activities probably by virtue of a toxophoric – N=C-S-Grouping. A large number of 4-thiazolidinones have been reported to be antifungal, antibacterial and antileukemic properties. These observations prompted us to synthesis the title compound with a presumption that incorporation thiadiazole and thiazolidinones would produce new compound with significant fungicidal properties. A series of 2-aryl-5-hydrazino-1, 3, 4- thiadiazole exemplified by the structure designed as analogue of the known vasodilator hydrazine and pyridazinyl hydrazine. Subsequent evaluation of this series showed that some analogue possessed both antihypertensive activity and anticonvulsant activity. Furthermore it found that particular substitution in the 2-position of aromatic ring to produced compound reduced with antihypertensive activity with desirable anticonvulsant activity. It was found that methylation of the α -nitrogen of the hydrazine group in the o-tolyl series decrease vasodilator activity without concurrent decrease in anticonvulsant activity[25].

heterobimetallic coordination polymers bis(1-ethoxycarbonyl-1-caynoethelene-2,2-dithiolato)cuprate(II) ion and $[MM'(cdc)_2]$, $[M = Zn(II), Cd(II), Hg(II); M' = Ni(II) \text{ or } Cu(II); cdc = \text{cyanodithioimidocarbonate}]$. All the complexes exhibited semiconducting behavior. Semiconducting properties of $Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II)$ and $VO(IV)$ complexes of Schiff base derived from resdiacetophenone and S-benzylidithiocarbazate were studied by Makode. It was found that complexes are semiconducting in nature[26].

Schiff base perhaps are synthesized in various method. In this paper, we will research which the simple way to synthesize Schiff base via compare of three primary methods. For the sake of convenience to compare the result, we choose the simple material (3,4,5-trimethoxybenzaldehyde and p-toluidine) to synthesize simple Schiff base[27].

This work describe the preparation new Schiff base and its some complexes derived from 4-amino antipyrine, sulphadiazine, and acetoacetanilide. The ligand is found to be chelating with metal ion in neutral tridentate manner through the azo methane nitrogen atoms and oxygen group of the acetoacetanilide[28].

Fifteen Schiff base from nicotino hydrazide with substituted aromatic benzaldehydes afforded title compounds (2a-n) and evaluated their *in vitro* antioxidant activity[29].

This paper describes the synthesis of a new Schiff base ligand containing a ring of pyrimidine and its metal complexes. Spectral and magnetic studies were used to characterize the structure of the complexes. IR, 1H -NMR, ^{13}C -NMR, and mass spectra were obtained to determine the structure of the ligand (HL). All of the synthesized compounds were evaluated for their antimicrobial activities against gram-positive and gram negative bacteria and fungi using the microdilution procedure .[30].

1,2,4-triazoles and their derivatives could be considered as possible antimicrobial agents, some of them studied in our laboratories In the present study, as a continuation of their studies on obtaining bioactive molecules, researchers have performed the synthesis of some new 1,2,4-triazole derivatives and investigation of antimicrobial activities of newly synthesized compound [31].

Azo dyes constitute one of the largest and most varied groups of synthetic organic dyes in this days [32]. Azo compounds are highly important, wellknown and widely used substances in the textile, paper, coloring agents for foods and cosmetics industries. Other applications include emerging technologies like liquid crystals, organic photoconductors and non-linear optics [33-34]. Azo compounds serve as important analytical tools by providing a strongly chromophoric label, the concentration of which is easily determined by

colorimetric, spectrophotometric or spectrofluorimetric methods. Besides, azo compounds are important analytical aid compounds serving as pH indicators, complexometric indicators and to a lesser extent, pre-concentration reagents [35]. The pharmacological use of azo compounds originates from the discovery of the antibacterial action of Prontosil on streptococcal infections by Dogmagk [36].

The scientists were synthesized by reacting $[Cu(Sac)_2(H_2O)_4] \cdot 2H_2O$ with the appropriate ligands in EtOH new mixed ligand complexes $[Cu(NNS)(sac)]$ ($NNS^I = S\text{-benzyl-}\beta\text{-N-(2-acetylpyrid-2-yl)methylenedithiocarbazate}$, $NNS^{IV} = S\text{-benzyl-}\beta\text{-N-(2-benzoylpyrid-2-yl)methylenedithiocarbazate}$ and $NNS^{II} = S\text{-benzyl-}\beta\text{-N-(6-methylpyrid-2-yl)methylenedithiocarbazate}$, $sac =$ the saccharinate anion). Magnetic and spectral evidence indicate that the complexes are four-coordinate in which the Schiff bases coordinate as NNS ligands and the sac anion coordinates as a unidentate N donor ligand. An X-ray crystallographic structural analyses of $[Cu(NNS^I)(sac)]$ shows that the complex has a distorted square-planar geometry with the Schiff base coordination to the $Cu(II)$ ion as a uninegatively charged. Tridentate chelating agent via the pyridine N atom, the azomethine N atom and thiolate S atom while the 4th coordination position is occupied by the N-bonded saccharinate anion[37].

$[Cu(qaldsme)(X)(MeOH)_n]$ and $[Ni(qaldsme)_2] \cdot 0,5 MeCN$ ($qaldsme =$ anionic form of the 2-quinoline carboxaldehyde Schiff base of S-methyldithiocarbazate; $X = NCS, J, NO_3^-$; $n = 0$ or (1)) were synthesized and characterized by magnetic and spectroscopic techniques. X-ray crystal structure determined of $[Cu(qaldsme)(ONO_2)(MeOH)]$, (1) $[Cu(qaldsme)(NCS)]$ (2) and $[Ni(qaldsme)_2] \cdot 0,5 MeCN$ (4) shows the nitrate complex of $Cu(1)$ is monomeric and five coordinate and the thiocyanato-complex (2) has a novel thilate S-bridged dimeric structure in which each of the $Cu(II)$ ions adopts a five coordinate approximately square-pyramidal geometry with a CuN_3S_2 coordination Kernel. The $Ni(II)$ complex (4) has a diistroted octahedral geometry with meridional disposition of the two uninegatively charged tridentate NNS ligands. In all these complexes, the Schiff bases are coordinated in their iminothiolate forms via the quonoline N atom, the azomethine N atom and the thiolate S atom [38].

New $Sn(IV)$ complexes of empirical formula, $Sn(NNS)_3$ ($NNS =$ anionic forms of the 2-quinolinecarboxaldehyde Schiff bases of -methyl- and S-benzylidithiocarbazate were prepared and characterized by a variety of physicochemtechniques. In the solid state, the Schiff bases exist as the thionate tautomer but it solution and in the presence of $Sn(IV)$ iodide they convert to the thiol tautomer and coordinate to the Sn atom in their deprotonated thiolate forms. The structures of the free ligand, H $qaldsbz$ and its triiodotin (IV) complexes $[Sn(qaldsbz)]_3$ were determined by X-ray diffraction [39].

Two new pyrimidine based NNS tridentate Schiff base ligands S-methyl-3-((2-S-methyl-6-methyl-4-pyrimidyl)methyl)dithiocarbazate [HL₁] and S-benzyl-3-((2-S-methyl-6-methyl-4-pyrimidyl)methyl)dithiocarbazate [HL₂] were synthesized by the 1:1 condensation of 2-S-methylmercapto-6-methylpyrimidine-4-carbaldehyde and S-methyl/S-benzyl dithiocarbazate. A Ni(II) complex of HL₁ and Co(II) and Fe(III) complexes of HL₁ were prepared and characterized by elemental analyses, molar conductivities, magnetic susceptibilities and spectroscopic studies. All the bis-chelate complexes have a distorted octahedral arrangement with an N₄S₂ chromophore around the central metal ion. Each ligand mol binds the metal ion using the pyrimidyl and azomethine N and thiolate S atoms (except in the Ni complex, one ligand mol uses the thione S in lieu of thiolate S atom). In the Ni(II) complex, one of the ligand mols behaves as a neutral tridentate and the other mol functions as a mononeg tridentate, whereas in the Co(III) and Fe(III) complexes, the ligand mols behave as monoanionic tridentate. All the complexes were analysed by single crystal x-ray diffraction and significant differences concerning the distortion from an octahedral geometry of the coordination environment were observed. [40]

New bis-chelated Zn^{II} and Cd^{II} complexes, [M(mpsme)₂](mpsm= the anionic form of the tridentate ONS donor ligand formed from Me pyruvate and S-methyldithiocarbazate) were prepared and characterized by conductance, IR, electronic and NMR spectroscopic techniques. Spectral evidence supports a six-coordinate distorted octahedral structure for these complexes. X-ray crystallography structural analysis also confirms that, in both the [Zn(mpsme)₂] and [Cd(mpsme)₂] complexes, the Me pyruvate Schiff base of S-methyldithiocarbazate is coordinated to the metal ions as a uninegatively charged tridentate ONS chelating agent via the carbonyl O atom, the azomethine N atom and the thiolate S atom. Both complexes are assigned a distorted octahedral geometry in which the ligands are arranged meridionally around the metal ions. The distortion from regular octahedral geometry is attributable to the restricted bite angles of the ligand. [41].

Condensation of SMDTC with 2-furyl-methylketone and 5-methyl-2-furaldehyde gave isomeric Schiff bases, (NS) and (NS¹). The metal complexes of these uninegatively charged bidentate Schiff base ligands with Cd, Sn, Fe, Pb, and Co were prepared. The complexes were characterized by a variety of physicochemical techniques. X-ray crystallographic analysis shows that the Cd(II) complex, bis [S-methyl-β-N-(2-furylmethylketone) dithiocarbazato] cadmium(II), consists of two mols with distorted octahedral structure. The Co(II) complexes are paramagnetic with a square-planar stereochemical. The diamagnetic Sn(II), Fe(III) and Pb(II) complexes also have square-planar structures while the diamagnetic [Cd(NS¹)₂] 3 H₂O complex is tetrahedral.

The [Cd(NS¹)₂] 3 H₂O, Sn(NS)₂ and [Co(NS)₂] showed clear inhibition of almost all bacteria and fungi tested. However, [Cd(NS)₂], [Fe(NS)] Cl₂, [Pb(NS)₂] and [Pb(NS¹)₂] were inactive against all bacteria assayed while [Cd(NS)₂], [Fe(NS)] Cl₂, [Pb(NS)₂] are very active against Human cell T-lymphoblastic leukemia (CEM-SS) and cervical cancer cell (HELA) with CD₅₀ values between 1.8 and 3.6 μL cm⁻³. [42]

Isomeric bidentate ligands having N-S donor sequence were prepared by condensing S-benzyl dithiocarbazate (SBTC) with 5-methyl-2-furylaldehyde (NS) and 2-furyl Me ketone (NS¹). {ML₂} (M=Pb, Fe, and Cd) and [ML₂] Cl_n (M=Sn, n=2 and Co, n=1) (HL=NS and NS¹) were prepared. The compounds were characterized by spectroscopic studies (IR, ¹H NMR and electronic spectra). X-ray crystallographic analyses of S-benzyl-β-N-(5-methyl-2-furylmethylene) dithiocarbazate shows two independent mols in the asymmetric unit. The mol adopts a trans-cis configuration, as was observed in other analogs, such as SBDC where the furylmethylene and benzyl groups are trans and cis about the N-C and C-S bonds, respectively. The mol structure of bis[S-benzyl-β-N-(2-furylmethylene) dithiocarbazato] cadmium (II) shows a tetrahedral geometry about the central Cd atom with the bidentate ligand coordinating through the thioketo S and the azomethine N atoms. The Pb(II) complex of the NS ligand was highly cytotoxic against leukemic cells (CEM-SS) with a CD₅₀ of 3.25 μg cm⁻³ while antimicrobial screening showed that the [Fe(NS)₂] Cl₂ H₂O complex was effective against *Aspergillus* ochraceus. [43]

Two new isomeric Schiff bases, S-methyl-β-N-(2-furylmethyl)methylenedithiocarbazate (NS¹) and S-methyl-β-N-(5-methyl-2-furyl)methylenedithiocarbazate (NS¹¹) were prepared. Bis-chelated complexes of these two bidentate ligands, [M(NS)₂], [M=Cu, Ni and Zn], were synthesized. The Schiff bases and their metal complexes were characterized by a variety of physicochemical techniques. X-ray crystallographic analysis shows that [Zn(NS¹)₂] is four-coordinate and has a distorted tetrahedral structure with the ligand coordinated to the Zn(II) ion as an uninegatively charged bidentate chelating agent via the azomethine N and the mercaptide S atoms. The Cu(II) complexes are paramagnetic with a square-planar stereochemistry. The Ni(II) and [Zn(NS¹¹)₂] complexes have a square-planar and tetrahedral structure, respectively, however, they are diamagnetic. Only Cu(NS¹)₂ showed clear activity against the bacteria, *Subtilis* mutant (B 28), while both NS¹ and NS¹¹ Schiff bases were strongly antifungal against *Saccharomyces cerevisiae* (20341). *Candida albicans*, *Candida lipolytica* (2075) responsibility. The Cu(NS¹)₂, Ni(NS¹)₂ and Zn(NS¹)₂ complexes showed very good activity against human cell T-lymphoblastic leukemia [CEM-SS] cells with CD₅₀ values of 1.6, 2.1 and 3.0 μg ml⁻¹, respectively. The remainder of the Schiff bases and complexes were inactive towards CEM-SS cells. None of the compounds showed any activity towards

colon cancer cells (HT-29). Only the $\text{Cu}(\text{NS}^1)_2$ and $\text{Zn}(\text{NS}^1)_2$ complexes were highly active against cervical cancer cells (HELA cells) with CD_{50} values of 1.5 and 2.1 $\mu\text{g ml}^{-1}$, while the $\text{Ni}(\text{NS}^1)_2$ complex was weakly active towards HELA cells with a CD_{50} value of 23.0 $\mu\text{g ml}^{-1}$ [44]

Four 5-coordinate $[\text{CuLQ}]\text{ClO}_4$ (HL= s-R- β -N-(pyridine N-oxide-2-ylmethylidene) dithiocarbazate (R=Me, CH_2 Ph): Q=o-phenanthroline (phen), 2,2'-bipyridine) were synthesized and characterized by UV, IR spectra and magnetic susceptibilities at room temperature. The x-ray crystal structure of $[\text{Cu}(\text{L})\text{phen}]\text{ClO}_4$ (R= CH_2Ph) was detected. The crystal structure contains a mononuclear unit in which Cu(II) displays a distorted square pyramidal geometry. Crystal data monoclinic, space group C2/c, a 19.227 (5), b 14.506 (3), c 20.487(4), β 106.00 (2), Z=8, $R=R_w=0.046$ [45].

New organometallic Sn(IV) complexes of the empirical formula $\text{Sn}(\text{NNS})\text{Ph}_2\text{Cl}$ (NNS= anionic forms of the 2-quinolinecarboxaldehyde Schiff bases of S-methyl- and S-benzylidithiocarbazate) were prepared and characterized by IR, electronic, ^1H NMR and ES mass spectroscopic techniques. The molecular structures of the 2-quinolinecarboxaldehyde Schiff base of S-methyldithiocarbazate (Hqaldsme) and its diphenyl tin (IV) complex. $\text{Sn}(\text{qaldsme})\text{Ph}_2\text{Cl}$, were detected, by x-ray diffraction. In the solid state, the ligand remains as the thione tautomer in which the dithiocarbazate chain adopts an E, E configuration and is almost coplanar with the quinolone ring. The $\text{Sn}(\text{qaldsme})\text{Ph}_2\text{Cl}$ complex crystallizes in two distinctly different conformationally isomeric forms, each having the same space group but different lattice parameters. X-ray analyses as a uninegatively charged tridentate chelating agent via the quinolone N atom, the azomethine N atom and the thiolate S atom. The two Ph groups occupy axial positions and the chloride ligand occupies the 6th coordination position of the Sn atom. The deprotonated ligand adopts an E, E, Z configuration in the complex. [46]

New mixed-ligand complexes of general empirical formula, $[\text{Cu}(\text{NNS})(\text{sac})(\text{H}_2\text{O})]$ (NNS= S-methyl- β -N-(6-methylpyrid-2-yl)methylenedithiocarbazate.

$\text{NNS}^{11}=\text{S-methyl-}\beta\text{-N-}[(2\text{-pyridyl})\text{phenylmethylene}]\text{dithiocarbazate}$, sac=saccharinate anion) were synthesized by reacting $[\text{Cu}(\text{sac})_2(\text{H}_2\text{O})_4]2\text{H}_2\text{O}$ with the appropriate ligands in water-EtOH mixtures and characterized by elemental analyses and conductance, magnetic, IR and electronic spectroscopic measurements. Magnetic and spectral evidence support a five-coordinate geometry for the complexes in which the Schiff bases coordinate as NNS tridentate ligands and the saccharinate anion coordinate as a unidentate N-donor ligand. An x-ray crystallographical structural analyses of $[\text{Cu}(\text{NNS}^1)(\text{sac})(\text{H}_2\text{O})]$ shows that the complex has a distorted square-pyramidal structure in which the Schiff base is coordinated to the Cu ion as a tridentate NNS chelating agent via the pyridine N atom, the

azomethine N atom and the thiolate S atom, the 4th and 5th coordination positions of the five-coordinate Cu(II) ion being occupied by the imino N of the saccharinate anion and O atom of the aqua ligand. The complexes were evaluated for their biological activities against eight pathogenic microbials and human T-lymphoblastic leukemia cell lines. The complexes exhibit marked cytotoxicity against leukemic cell lines and display moderate activity against pathogenic bacteria and fungi [47].

New mixed-ligand Cu(II) complexes of empirical formula $[\text{Cu}(\text{pysme})(\text{sac})(\text{MeOH})]$ and $[\text{Cu}(\text{6mptsc})(\text{sac})]_2$ were synthesized and characterized by conductance, magnetic, IR and electronic spectroscopic techniques. X-ray crystallographical structure analyses of these complexes indicate that in both complexes the Cu(II) ions adopt a five-coordinate distorted square-pyramidal geometry with an N_3SO donor environment. The Schiff bases are coordinated to the Cu(II) ions as tridentate NNS chelates via the pyridine N atom, the azomethine N atom and the thiolate S atom. In the monomeric $[\text{Cu}(\text{pysme})(\text{sac})(\text{MeOH})]$ complex, the saccharinate anion acts as a monodentate ligand coordinating the Cu(II) ion via the imino N atom whereas in the dimeric $[\text{Cu}(\text{6mptsc})(\text{sac})]_2$ complex, the sac anion behaves as a bridging bidentate ligand providing the imino N donor atom to one of the Cu(II) ions and the carbonyl O as a weakly coordinated axial ligand providing the imino N donor atom to one of the Cu(II) ions and the carbonyl O as a weakly coordinated axial ligand atom to the other Cu(II) ion. In both complexes the Cu(II) ions have distorted square-pyramidal environments. The distortion from an ideal square-pyramidal geometry is attributed to the restricted bite angles of the planar tridentate ligand [48]

Condensation of SMDTC with 2-furyl-methylketone and 5-methyl-2-furaldehyde gave isomeric Schiff bases, (NS) and (NS¹). The metal complexes of these uninegatively charged bidentate Schiff base ligands with Cd, Sn, Fe, Pb and Co were prepared. The complexes were characterized by a variety of physicochemical techniques. X-ray crystallographic analyses shows that the Cd(II) complex, bis[S-methyl- β -N-(2-furylmethylketone)dithiocarbazato]cadmium(II), consists of two molar with distorted octahedral structure. The Co(II) complexes are paramagnetic with a square-planar stereochemistry. The diamagnetic Sn(II), Fe(III), and Pb(II) complexes also have square-planar while the diamagnetic $[\text{Cd}(\text{NS}^1)_2] 3 \text{H}_2\text{O}$ complex is tetrahedral. The $[\text{Cd}(\text{NS}^1)_2] 3 \text{H}_2\text{O}$, $[\text{Sn}(\text{NS})_2]$ and $[\text{Co}(\text{NS})_2]$ showed clear inhibition of almost all bacteria and fungi tested. However, $[\text{Cd}(\text{NS})_2]$, $[\text{Fe}(\text{NS})\text{Cl}_2]$ and $[\text{Pb}(\text{NS})_2]$ showed clear inhibition of some fungi. The $[\text{Cd}(\text{NS})_2]$, $[\text{Cd}(\text{NS}^1)_2]3 \text{H}_2\text{O}$ and $[\text{Co}(\text{NS})_2]$ are very active against Human cell T-lymphoblastic leukemia (CEM-SS) and cervical cancer cells (HELA) with CD_{50} values between 1.8 and 3.6 $\mu\text{L cm}^{-3}$ [49]

A new dithiocarbamate ligand, S-2-picolylidithiocarbamate (S2PDTC) was synthesized using 2-picolyl chloride hydrochloride. Tridentate Schiff base were prepared by condensation of S-2-picolylidithiocarbamate (S2 PDTC) with pyridine-2-carboxaldehyde (NNS¹), 2-acetylpyrrole (NNS¹¹) and 2-acetylthiophene (NSS), while a bidentate Schiff base (NS) was prepared by condensing the S2 PDTC with 2-acetylfuran. Complexes of S2 PDTC and its Schiff bases with Ni(II) salts were synthesized and characterized by elemental analyses and various physicochemical techniques. A square-planar structure is proposed for the diamagnetic [Ni(S2 PDTC)₂] and [Ni(NSS)₂] complexes while [Ni(NS) Cl] complexes was dimeric. All of the Ni(II) complexes were inactive against CEM-SS cancer cells.[50]

In the next work describes synthesis of hydrogen-bonded pseudo-dimer, [Mn(III)L₁(CH(3)CH(2) OH) (2) (Cl O(4)) (1) (L₁=N, N¹-bis (2-hydroxy-1-naphthalidenato)-1,2-diaminopropane) has been synthesized. The single crystal X-ray diffraction reveals that the structure affords an elongated octahedral MnN (2) O(4) coordination environment, geometry with the four donor atoms of the tetradentate Schiff base in the equatorial plane and with two ethanol molecule in axial positions with Mn-O=2.265 (2) and 2.266 (2) Å [51].

In this research we report on the study of hydrogen bonds of the Schiff base and water molecules in D85 S in the absence and presence of various halides, assigning their N-D and O-D stretching vibrations in D (2) O, respectively in low temperature Fourier transform infrared (FTIR) spectroscopy. They found that the hydrogen bond of the Schiff base in D85S (Cl(-)) is much stronger than that in HR, being as strong as that in wild-type BR [1017].

The next work describes the synthesis of Schiff bases containing pyridoxal (PL), N-(pyridoxylidene)tolylamine, C(15) H (16) N(2) O (2) (I), N-(pyridoxylidene)-methylamine C(9) H (12) N(2) O(2) (III) and their 1:1 adduct with 2-nitrobenzoic acid, (I) (+) C(7) H (4) NO₂: - (II) and 4-nitrobenzoic acid (III) (+) C(7) H (4) NO₂: (IV) serve as models for the coenzyme pyridoxal 5¹-phosphate (PLP) in its PLP-dependent enzymes. These models allow the study of the intramolecular OHN hydrogen bond of PL/PLP. Schiff bases and the H-acceptor properties of their rings. The proton in the intramolecular O-H.N hydrogen bond of (I)/ (III) is located close to oxygen (enolamineform) [52].

In this work describes low temperature Fourier transform infrared (FTIR) spectroscopy to the all-trans form of ASK at 77 K, and compared the local structure around the chromophore and their structural changes upon retinal photoisomerization with those of BR. Scientist determined that the weak hydrogen bond of the bridged water between the Schiff base and Asp 75 originates from their geometry [53].

The synthesis, and structural characterization of seven heterodinuclear complexes (1); [Cu^{II}(HL)Na^I

(NO₃)(MeOH)] (1), [Cu^{II}(HL)Pb^{II}(NO₃)₂] (6) and [Cu^{II}(HL)Cd^{II}(NO₃)₂] (7) are reported, where H₃L=9=N,N¹-bis(3-methoxysalicylaldimine)-1,3-propylene-2-ol.

Compounds 1 and 3 crystallize in the monoclinic P 2₁/n space group, 4,5 and 7 in the monoclinic P 2₁/c space group, while the space group of complexes 2 and 6 is triclinic P₁. The X-ray crystallography, reveals that the structures of all the complexes consist of dephenoxo-bridged heterometallic cores in which Cu^{II} metal ion is trapped in N₂O₃ compartment of the Schiff base ligand while the second metal ions present in the larger and open O₄ [O(phenoxo)₂ O(metoxo)₂] compartment [54].

[Cu₃(TFSSB)₂(H₂O)₄ 4 H₂O]_n (TFSSB= taurine 3-formylsalicylic acid Schiff) was synthesized from TFSSB and Cu(II) acetate monohydrate in EtOH solution and the crystal structure was detected by x-ray diffraction method. The crystal belongs to monoclinic system, space group P2₁/n, with a=0,9279 (6) nm, b=1.1730 (2) nm, c 1.471 (2) nm, β 106.96 (2), V= 1.531 (2). Z=2, d_c=1.890 cm⁻³, μ=2.291 mm⁻¹, F(000)=882, R₁= 0.0259, wR₂= 0.0659. The Cu 1 is five-coordinate, the Cu2 is four-coordinate. [55]

Two new Schiff base macrocycles-a 4+4 condensation product and a meso-type 2+2 condensation product-were obtained in a reaction of trans-1,2-diaminocyclohexane and 2,6-diformylpyridine. Reduction of these compounds led to the corresponding 4+4 and 2+2 macrocyclic amines. The macrocycles were characterized by NMR spe

ctroscopy and electrospray mass spectrometry. The symmetry and stereochemical of these macrocycles, as well as of new 3+3 and 4+4 diastereomers identified in solution., has been established. X-Ray structures of the 2+2 and 4+4 Schiff basemacrocycles confirm the configurations detected on the basis of spectroscopic investigations. The crystal structure reveal that the centers of the square-shaped 4+4 macrocycles form channels as a result of columnar stacking.[56].

Distribution of the electric charge in electro- and photoactive polymers poly [Msalen] and poly[MSalbn] (M=Cu(II), Ni(II), Pd (II), Salen= bis(salicylidene)ethylenediamine: Salbn=1,4-bis(salicylidene-1,4-butylenediamine) was studied using XPS. The results of comparative analyses of the binding energy of the inner 1 s-electrons of functional N and O atoms were discussed. Distribution of electron d. in free ligands, in complex monomers and corresponding polymers are also discussed. Intramolecular charge transport and electric conductor of a structural unit of poly [MSalen] were discussed.[57].

New series of macrocyclic Schiff base lanthanide (III), Y(III) and Cd(II) complexes [M(1)]X_n (X=NO₃⁻, M=Y, Ln=La-Yb except Pm and Dy; X=ClO₄⁻, M=Cd, La, Ce, Pr, Sm, Gd, or Er) and [M(3)] X_n (X=NO₃⁻, M=Dy; X=ClO₄⁻, M=Er and Cd), were prepared by cyclocondensation of O¹, O⁷-bis (formylphenyl)-1,4,7-trioxahptane (1) Or tris (2-aminoethyl)amine (3) in the

presence of the appropriate metal salt as a template agent. The Schiff-base macrocycles 1 and 3 are also formed in the absence of a metal ion. Treatment of 1 with NaBH_4 in MeOH gives the diamine macrocycle 2. The reactions of Ln^{III} , Cd^{II} and Y^{III} ions with 2 also were studied. The crystal structures of monoprotonated 2 and of $[\text{Cd}(3)](\text{ClO}_4)_2$ were detected by x-ray diffraction analyses.[58].

Furan-2,5-dicarboxaldehyde with $[\text{H}_2\text{NXO}(\text{CH}_2)_2]_2\text{O}$ [$\text{X}=1,2\text{-C}_6\text{H}_4, (\text{CH}_2)_2$] in EtOH or BuOH in the presence of MSCN ($\text{M}=\text{Ca}, \text{Sr}, \text{Ba}$) gave the corresponding macrocycles. The structure of 1 [$\text{X}=(\text{CH}_2)_2, \text{M}=\text{Sr}$] was detected by x-ray crystallography[59].

A new di-Schiff base ligand was prepared from 3-acetylpyridine and 1,2-diaminoethane and its structure also was characterized by single crystal x-ray diffraction. Also, the ligand forms a 1:1 complex with Ag (NO_3) in MeCN. The crystal structure of the complex exhibits a 1-dimensional-double helix with the pitch length of 10 Å. In these reactions, the ligand was found to disintegrate into the individual components to form a crystal of a 3-dimensional-network which comprised of Ag (NO_3) and 1,2-diaminoethane. Nitrate ions occupied the channels and form several N-H...OH bonds with the walls of the channels. The topology of the 3-dimensional-network is similar to that of the CdSO_4 . This structure prompted the authors to study the reactions of Ag (NO_3) with 1,2-diaminoethane, 1,2-diaminopropane and 1,3-diaminopropane. The crystal structures of these complexes reveal that 1,2-diaminopropane and 1,3-diaminopropane and 1-dimensional-zigzag chain, structure.[60].

Nowadays we know that, there is no possibility recovering all of disease without binding DNA. Some of complexes Schiff bases show DNA binding properties they can bind DNA through intercalation with the binding concentration at the order of different magnitude. In this work scientists have been synthesized new Ho complexes of Schiff-base ligands derived from 8-hydroxyquinoline-2-carboxyaldehyde and arylhydrazines. Studying of DNA binding properties showed that all the ligands and Ho(III) complexes can bind to Calf thymus DNA through intercalation with the binding const. at the order of magnitude $10^5\text{-}10^6 \text{ M}^{-1}$, but complexes present stronger affinities to DNA than ligands. It has been written that all complexes may be used as potential anticancer drugs [61].

It has been reported synthesis of new $\text{N,N}'$ -bis(3,5-tet-butylsalicylidene-2-hydroxy)-1,3-propanediamine substituted binuclear Cu(II) complexes. All synthesized complexes can cleave plasmid DNA to nicked DNA in a sequential manner as the concentration or reaction times are increased in the absence of reducing agent. Their cleavage activities are promoted in the presence of H_2O_2 . They showed that cleavage mechanisms between the complexes and plasmid DNA probably involve singlet

oxygen $^1\text{O}_2$ and OH as reactive oxygen species used[62].

Next work also reported binuclear Cu(II) complexes derived from salicylaldehyde and 2-mercaptoethylamine. Investigation shows that the complexes behaving photo-induced cleavage of supercoiled pUC 19 DNA in UV light of 365 nm and red light of 633 nm (He-Ne laser). The DNA photocleavage reaction involves formation of singlet oxygen ($^1\text{O}_2$) as the reactive species in a type-II pathway[63].

In this work described the synthesis of oxovanadium complexes derived from $\text{N,N}'$ -dimethylenediamine and *o*-hydroxy-acetophenone. Scientist also investigated DNA binding ability and photoinduced DNA cleavage activity. The complex binds to double-stranded DNA giving a K_{aa} value of $1.56 \times 10^7 \text{ M}^{-1}$ and displays DNA cleavage activity on UV (300 nm) irradiation via a mechanistic pathway involving formation of singlet oxygen as the reactive species[64].

In other works, shown synthesis of Cd (II) complexes derived from 2,6-bis[1-(94-amino-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxypyrimidin-5-yl)-imino]ethylpyridine. After investigation electrophoretic experiments indicate that the Cd complex induces cleavage of the plasmid pBR322 DNA to give ulterior nicking and shortening of this mol. AS a result of the complex binding to DNA, resulting in the conclusion that 1 behaves as a chemical. Nuclease. Cytotoxic activity of the Cd(II) complex against selected different human cancer cell lines is specific and increases with increasing concn medium is supplemented with. 1 a remarkable inhibition of the growing cell is obsd., important cell degeneration appears before 48 h and abundant ppts. Are formed that correspond to cell residues and denatured proteins[65].

Next work investigate the synthesis of new ternary Cu(II) complexes derived condensation of 2-mercaptoethylamine hydrochloride with salicylaldehyde or 2-hydroxy-3-methoxybenzaldehyde. Complexes show DNA cleavage activity. The complexes exhibit quasireversible cyclic voltammetric response in DMF-Tris buffer for the Cu(II)/ Cu(I) couple. [66].

New Copper (II) of different nuclearities viz $[\text{Cu}(\text{salmet})(\text{bpy})]$ (1), $[\text{Cu}(\text{salmet})(\text{HIm})_2]$ (2) and $[\text{Cu}(\text{salmet})(1\text{-Melm})]$ (3), where salmet is dianionic Schiff base *N*-salicylidene-*L*-methioninato, were prepd., structurally characterized by x-ray crystallog. and their hydrolytic DNA cleavage activity studied. The copper complexes show significant DNA cleavage activity in the dark giving an order $1 > 3 > 2$. The hydrolytic nature of the DNA cleavage is evidenced from the control expts. Showing no apparent inhibition of cleavage under argon atm. And in the presence of hydroxyl radical inhibitor DMSO or singlet oxygen quencher azide ion[67].

In this part of research we have showed the antimicrobial properties of Schiff bases. We are going to describe different scientific research about Schiff bases antimicrobial properties.

First research devoted to studying of antimicrobial properties of 5-methylpyrazole-3-yl-N-(2-hydroxyphenylamino)methylene and its complexes (Co(III), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II)). Researchers have described in vitro antimicrobial activity of ligand and the metal complexes and it have been studied by SEM against some pathogenic bacteria [68].

The next work were described synthesis and antimicrobial properties of 2-(E)-(4-methoxyphenylimino)phenol and the metal complexes (Mn(II), Co(II), Ni(II), Cu(II) and Zn(II)). The antimicrobial activity investigation shows that Mn(II) and Zn(II) show against the species *Aspergillus niger* higher antifungal activity [69].

In this work were studied synthesis, characterization, 2-((E)-(2,4-dibromophenylimino)methyl)-4-bromophenol and the complexes (Cu(II) and Ni(II)). The investigation of antimicrobial properties were investigated against two bacteria (*E. coli* and *Salmonella typhi*) and two fungi (*Penicillium*, *Aspergillus* sp). They have been determined that the complexes show more biological activity than the Schiff base [70].

The next work shows synthesis and urease inhibition of Schiff bases derived from isoniazid and fluorinated benzaldehyde and their copper complexes. All synthesized compounds were evaluated for their antimicrobial activity and urease inhibition. All copper (II) complexes showed excellent inhibitory properties against jack bean urease, considerably better than that of the standard acetohydroxamic acid [71].

The next report was described synthesis of 2-((E)-(2-pyridine-2-ylthio)ethylimino)methylphenol substituted Co(II) and Ni(II) complexes. Study antimicrobial properties determines that this compounds show antibacterial activity as well as catecholase activity [72].

Trimethylsilyl-propyl-p-aminobenzoate and its Cu(II), Zn(II) complexes were synthesized. The antifungal and antibacterial properties of the prepared compounds against *Aspergillus fumigatus* ATCC 66567, *Penicillium chrysogenum* ATCC 20044, *Fusarium* ATCC 20327 *Bacillus* sp ATCC 31073, *Pseudomonas* sp. ATCC 15780 were evaluated/ Both Schiff bases and metal complexes showed better antimicrobial activity compared to the standard compounds Caspofungin and Kanamycin [73].

2,2'-bis((E)-azanediy bis (propane-3,1-diyl))bis (azanylidene) bis (methanylidene) dephenol substituted Ni(II), Zn(II), Fe(II) and Cu(II) was synthesized. Antibacterial activity of ligand and its transition-metal complexes was studied using disk diffusion assay. Zn(II)-1 and Ni(II)-1 exert a high

inhibition of the growth of all bacterial strains with inhibition diameters ranging from 8 to 14 mm [74].

S-allyl-2-(4-benzyloxyphenylmethylene) hydrazinecarbodithioate substituted Ni(II), Cu(II), Zn(II), Cd(II), Pd(II) complexes was synthesized. The in vitro bactericidal activity suggests that the palladium (II) complex is strongly active against two bacteria. The cadmium (II) complex is moderately cytotoxic with an LC₅₀ value of 409 µg/ml [75].

The Schiff bases ligand, 1-phenyl-3-methyl-5-hydroxypyrazole-4-methylene-8¹-quinolineimine and its Cu(II), Zn(II) and Ni (II). The ligand and its metal complexes were subjected to cytotoxic test and the metal complexes show significant cytotoxic activity against lung cancer A 549 cell [76].

It have been synthesized N,N¹-bis(2-hydroxy-1-naphthaldehyde)-1,2-phenyldiamine; L₂-N,N¹-bis(salicylidene)-1,2-phenyldiamine, L₃-N,N-bis(5-*l*-salicylidene)-1,2-phenylenediamine: 4,4¹-bpy=4,4¹ bipyridene and their metal complexes. Researchers determined that the ferromagnetic interaction observed in second complex is tentatively ascribed to the dimer formation through Fe-π interaction at low temperature [77].

The next work was described the synthesis of five new octahedral Fe(II) complexes [FeL₂(4-dpa)]_n (EtOH) (1), [FeL₂(bipy)]_n(DMF) (2). All compounds are characterized using x-ray structure analyses and T-dependent susceptibility measurement. Both methods indicate that all Fe(II) are in the paramagnetic high-spin state over the whole temperature range studied. The O-Fe-O angle, the so called bite of the equatorial ligand, is with an average of 111° in the region typical for high spin Fe(II) complexes of this ligand type. In the case of compound 1 and infinite two-dimensional H bond network can be found for the compounds second and fourth H bond interaction are observed between the complexes molecules. A comparison of the curve progression obtained from the magnetic measurements of the mononuclear complex fifth and the polymeric complexes 1-3 indicated that no magnetic interactions are mediated over the bridging axial ligands. For the dinuclear complex 4 weak antiferromagnetic interactions between the two Fe centers are found [78].

Five binuclear Schiff base Cu(II) complexes [Cu₂(L)(OAc)]₃ DMF (1) [Cu₂(L)(OAc)]₂ 3 DMF (2), [Cu₂(L)(BNPP)]₃ MeCN (3), [Cu₂(L)(Fa)]₂ DMF (4), [Cu₂(L)(Pa)] DMF (5), (H₃L= N,N¹-bis(3,5-tert-butylsalicylidene)-2-hydroxy)-1,3-propandiamine, BNPP=bis(4-nitrophenyl) phosphate, Fa=2-tetrahydrofuroate acid Pac=benzoate) were synthesized and characterized by x-ray single-crystal structure analyses. Variable temperature magnetic susceptibility studies (2-300 K) indicate the existence of ferromagnetic coupling between the (II) ions complexes 1 and 4 antiferromagnetic coupling in complexes 3 and 5. [79].

Three cyanide-liked Fe(III), Mn(III) bimetallic clusters, [(Tp) Te (CN)₃]₂ [Mn(aacphen)], [1: acphen=N,N¹-ethylenebis(2-hydroxyacetophenylideneiminato) dianion, [(Tp (Fe (CN)₃), [Mn (5-bracphen)], [2: 5-bracphen= N,N¹-ethylenebis (5-bromo 2-hydroxyacetophenylidene iminato) dianion] were prepared, by self-assembling a facial [(Tp)Fe (CN)₃], [Tp= hydrolysis (pyrazoly) borate] precursor and responsible Mn(III), Schiff bases. Although the geometric parameters relevant to the magnetic Fe-C=N-Mn pathways are analogous to each other their magnetic natures are varied across the compounds, which support that a degree of orbital overlap is quite sensitive to a subtle structural change in the present system [80].

Researcher have been synthesized {Cr(CN)₄ [CNMn(salen) (MeOH)]₂[Mn(salen)(CH₃OH)(H₂O)]} [Mn(salen)(MeOH)]₂ [Cr(CN)₆]-6CH₃OH (1; H₂ salen= N,N¹-ethylenebis(salicylidene-amine)) ligand and their complexes. All these structural units are linked by hydrogen bonds into a 3 D network. The magnetic characterization shows that first complex displays a weak ferromagnetic behavior [81].

The next work describes synthesis of four trinuclear Cu(II) complexes, [CuL¹]₃ (μ-OH)](NO₃)₂](1), [CuL²]₃ (μ-OH)](I)₂ H₂O](2), [CuL³]₃ (μ-OH)](I)₂](3),

and [CuL¹]₃ (μ-OH)](CuI)₂](4), where HL¹ (8-amino-4-methyl-5-azaoct-3-en-2-one), HL² [7-amino-4-methyl-5-azaoct-3-en-2-one] and HL³ [7-amino-4-methyl-5-azahept-3-en-2-one] are the three tridentate ligands and characterization.

Magnetic susceptibilities were determined for these complexes at 2-300 K. The isotropic Hamiltonian, H=J₁₂S₁S₂-J₁₃S₁S₃-J₂₃S₂S₃ was used to interpret the magnetic data. The best fit parameters obtained are J=- 54,98 cm⁻¹, g=2,24 for 1; J=-56,66 cm⁻¹, g=2,19 for 2; J=-44,39 cm⁻¹, g=2,16 for 3; J=- 89,92 cm⁻¹, g=2,25 for 4. The EPR data at low temperature indicate that the phenomenon of spin frustration occurs for complexes 1-3 [82].

Researcher were synthesized two new azido derivatives of tridentate Schiff base copper (II) complexes. Analyses reveals that [Cu(L¹) (N₃)J (1), containing 1-(salicylideneimino)-2-(diethylamino) ethane (HL¹) as coligand is monomeric in nature while complex [Cu(L₂) (N₃) J_n (2) containing, 1-(salicylideneimino)-2-(dimetyamino) ethane (HL₂) as coligand, has a 1-dimensional infinite chain structure in which copper (II) is square planar in the case of complex 1 ç base ligand (HL¹) and the fourth site is occupied by an azido group. However, in complex 2 the copper(II) is square planar in the case of complex 1, base ligand (HL₁) and the fourth site is occupied by an azide group.

However, in complex 2, the copper (II) coordination is distorted square pyramidal. The four in -plane coordination sites are similar to those in complex 1. The fifth apical coordination is provided by a nitrogen atom of the azido group of a symmetry related moiety

with a long Cu-N bond distance, resulting in the polymer of the complex. The variable temperature magnetic susceptibility measurements showed that the magnetic interaction in [Cu(L₂) (N₃) I_n (2) is antiferromagnetic (I=-22,5 (±0.2) sm⁻¹) while as expected [Cu(L₁) (N₃) I (1) is paramagnetic. The solvent electronic spectra of the complexes show strong absorption bands associated with N₃ Cu(II) charge transfer transition [83].

An iron complex [Fe (H₅L)] Cl₃, of a hexadentate linear Schiff base ligand (H₂L) containing O₂N₄ donor atoms bis (salicylidene) triethylenetetramine, was prepared from FeCl₃ and the structure determined with x-ray diffraction. The Fe(II) ion in the reactant is oxidized to form the Fe(III) complex. [C₂₀H₂₄Cl₃N₄O₂] Fe, and the three chloride ions are situated at distance of Fe. Cl(1) 3.976 (5), Fe. Cl(2) 4.479 (3) and Fe. Cl(3) 7.509 (4). A outside the coordination sphere. The Fe(III) ion has an octahedral coordination sphere and as expected the tuo oxygen donor atoms are coordination in a as positionş The Fe-Oç Fe-N_{imin} and Fe-N_{amine} distances are 1.880 (3) Å 1.931 (4) Å and 2.004 (4) Å, responsibility [84].

The next work describes the synthesis of [Na₂L₂(μ_{1,1}-N₃)₂ (N₃)₂] complexes in the base of reaction between Ni(NO₃)₂ 6 H₂O with L in the presence of excess of sodium azide in methanol at room temperature. Here L is N,N-bis (2-pyridylmethyl amine) (L₁) and N-(2-pyridylmethyl-N¹, N¹-diethylethylenediamine (L²). The x-ray structure of both compounds reveal that the N₁N₁N coordinating reduced Schiff bases are legated facially. The N₁-N_{azido}-Ni angle is-100⁰ and the Ni.Ni seeepn. Is 3.2 H. The variable temperature magnetic susceptibility measurements of the two complexes show ferromagnetic behavior [85].

Researchers were synthesized three cubane copper (II) cluster, [Cu₄(HL¹)₄] (1) [Cu₄L₂(OH)₂] (2) and [Cu₄L₂(OMe)₂] (3) of two pentadentate Schiff base ligand N₁N¹-(2-hydroxypropane-1,3-diyl) bis (acetylacetoneimine) (H₃L¹) and N₁N¹-(2-hydroxypropane-1,3-diyl) bis (salicylaldimine) (H₃L), and magnetic properties studied.

The variable temperature magnetic susceptibility exchange pathway, there is also a weak antiferromagnetic exchange between the copper centers. The theory fitting of the magnetic data gives the following parameters: I₁=38,5 and I₂=- 18 cm⁻¹ for 1 with a triplet (S=1) ground state and quintet (S=2) lowest excited state; I₁= 14,7 and I₂= -18,4 cm⁻¹ for 2 with a triplet ground state and singlet (S=0) lowest excited state; and I₁=33.3 and I₂=- 15,6 cm⁻¹ for 3 with a triplet ground state and quinted lowest excited state, where I₁ and I₂ are two differet exchange pathways in the cubane ground state and quinted lowest excited state, where I₁ and I₂ are two different exchange pathways in the cubane (Cu₄O₄) core. The crystal structures of 26 H₂O and 32 H₂O. THF show channels containing the lattice solvent mols [86].

We have also been synthesized different substituted Schiff bases and its metal complexes. In our experimental research time we have obtained that all azomethines show antimicrobial properties [87].

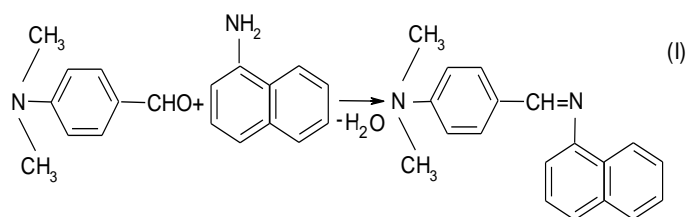


Fig 4. P-dimethylaminobenzylidene- α -naftylamine

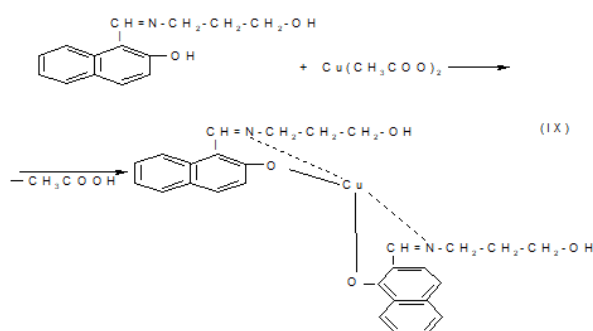


Fig 5. Cu-bis[P-dimethylaminobenzylidene- α -naftylamine]

From the picture we can see production of p-dimethylaminobenzylidene- α -naftylamine (Fig 1). This ligand show high bactericidal and fungicidal properties. The positive side of this research is ligand and metal complexes (fig 2) in very few concentration maintain their properties.

When we increased the application field observed that these compounds show multifunctional properties. [88,89]. In this researches show antimicrobial, antioxidant, anticorrosion properties of schiff bases and metal complexes. The positiveness of this work is these compounds maintain their properties very long time (6 months).

Nowadays we started new ways the synthesis side of azomethines such as the synthesis of buffer solutions [90]. In future we will investigate the azomethines in the drug chemistry.

Conclusion.

Schiff bases have been widely explored for industrial applications. However, the biological activity of this class of compounds deserves further investigation. This becomes clear when plant pathogens are considered. Although the research on this subject is incipient, a number of reports disclosing the effects of the Schiff bases on the pathogens of clinical interest have recently been increasing. Schiff base compounds have been shown to be promising leads for the design of more efficient antimicrobial agents. Advances in this field will require analyses of the structure–activity relationships of the

Schiff bases as well as the mechanism of action of these compounds. The synthesized of Schiff bases have been reported in the above reviewed work gives different approaches to the challenge of preparing these bioactive products and allows the synthesis of many novel chemical derivatives. These derivatives have vast range of biological activities which benefits us.

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