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Antimicrobial, electrochemical and thermodynamic studies of Schiff base complexes and their potential as anticarcinogenic and antitumor agents: A review

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Abstract: *The present paper is an overview of different methods of synthesis of Schiff bases and their complexes from different set of amino and carbonyl compounds, the applications of Schiff base complexes as antimicrobial, antifungal, antibacterial, antipollutant, anti tumour and anticarcinogenic, which also includes the activity of Schiff base complexes widely utilized to analyze some physical parameters of compounds like pH, electrochemical and thermodynamic studies. Recently these metal complexes are also extensively used in pharmaceutical industry. Therefore the present paper is concerning the different aspect of synthesis and wide scope of application of Schiff base complexes.*
Keywords*: anticarcinogenic, antitumor, pH, electrochemistry, thermodynamics*

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I. Introduction

Metal complexes of Schiff bases have played a fundamental role in the advancement of co-ordination chemistry. Schiff bases present adaptable and supple sites of ligands proficient to attach with a variety of metal ions to offer complexes with appropriate properties for hypothetical and practical applications.

Metal chelates of N and S chelating ligands have concerned significant consideration because of their remarkable physicochemical properties and prominent biological activities. The N and S atoms perform a crucial role in the coordination of metals in several metallobimolecules. The Schiff bases (containing azomethine linkage) are found to be most appropriate ligand by many researchers for the coordination complexes due to its notable ability of coordination through N and S atoms (sometimes oxygen also). By the donation of lone pair of electrons of Schiff base, the hybridization of vacant orbital of metal occurs and coordination complex is formed. Some significant transition metals also demonstrate micro nutrient properties and participate in essential biological functions in animal and plant kingdom. Extensive research on these complexes has revealed significant evolution in utilization of metal complexes as drugs to treat numerous human diseases like carcinomas, lymphomas, infection control, anti-inflammatory, diabetes and neurological disorders. Moreover Schiff base complexes have also been extensively considered for electrochemical [Guo et al 2008], thermodynamic studies [Guo et al 2013].

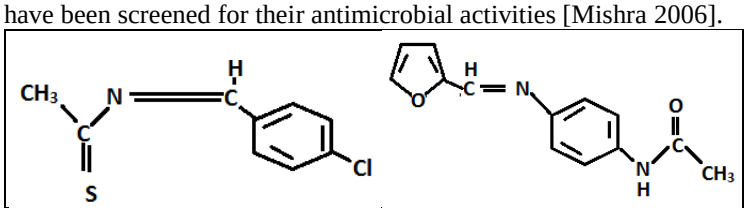
The metal complexes containing heterocycles like thiazole are found to be component of many pharmacologically and biologically active compounds. For instance compounds containing benzothiazole and sulphonamide derivatives were reported to be antifungal [Chavan and Pae 2007, Sushil kumar and Devanad 2003], anti-inflammatory [Racane et al 2001], antiHIV [Caleta et al 2004], anticancer[Supuran & scozzafava 2000], anticarbonic anhydrase [Hasan et al 2004], [Neelakanthan et al 2010] and in therapeutic fields. In the present review attempts have been made to describe the wide applications of Schiff bases and their complexes in various imperative fields.

II. Various Applications of Schiff base complexes

2.1 Antimicrobial studies of Schiff bases:

The innovation in the field of bio-inorganic chemistry has enhanced the concern of the scientists in the coordination complexes of schiff bases, since it has been previously recognized that many of these complexes can be used against many microbial species. Consequently, we account the biological activities of these complexes as follow:

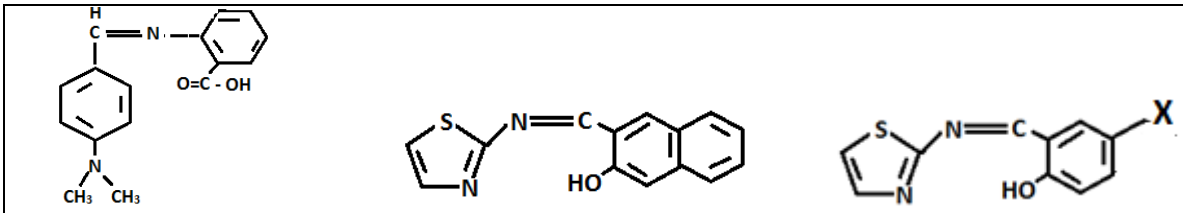
The condensation product of thioacetamide or 4-aminoacetanilide with furfuraldehyde or 4-chlorobenzaldehyde (scheme 01) is a Schiff base ligand. The complexes of cobalt, nickel and copper with Schiff base synthesized, have been screened for their antimicrobial activities [Mishra 2006].



Scheme 01

Another tridentate Schiff base p-dimethylamino benzylidene anthranilic acid (PDBAA) derived from p-dimethyl aminobenzaldehyde and anthranilic acid and their solid complexes of Mn(II) and Fe(II) have been reported to show antigungal and antibacterical activities and screened against several fungi and bacteria (scheme 02). The metal chelates have a general formula [MCPDBAA) $(H2O)_3$] M=Mn(II) or Fe(II) [Mehta et al 2006].

Similarly the complexes of Schiff bases synthesized from substituted 2-aminothiazole and substituted salicylaldehyde & 2-hydroxy 1-naphthaldahyde are found to exhibit antibacterial and antifungal activities. The structures of these chelates were recognized by analytical and spectral data. Some of metal complexes were found potent against selected bacteria and fungi [saxena 2004] and [Mehta et al 2007].

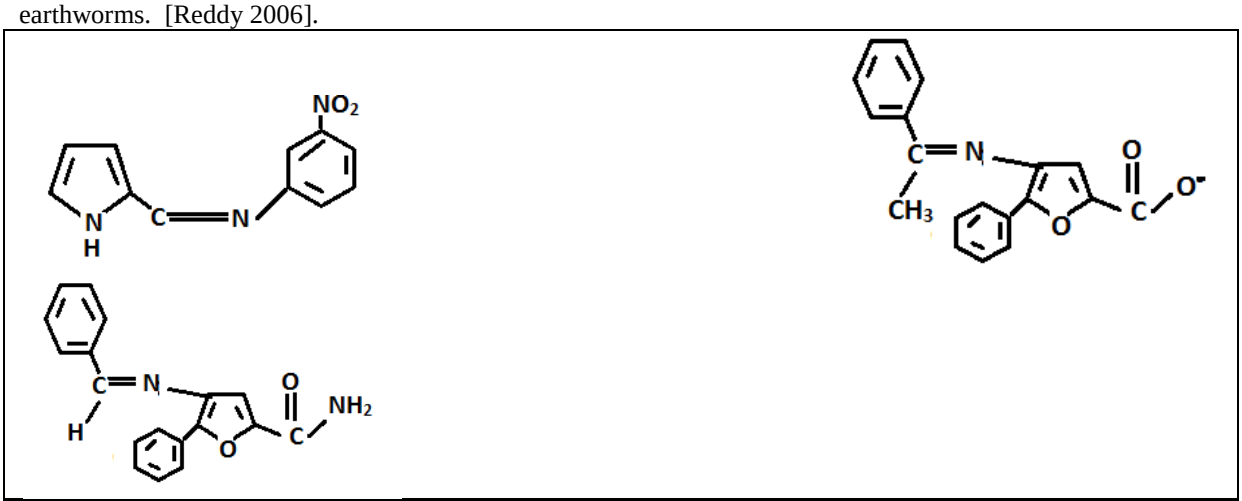


Scheme 02 **scheme 03**

The complexes of the type [n2-C_2H_5)2HfL] (L=Schiff base ligand (LH_2), resulting by condensing benzyl α monoxime and aromatic and aliphatic diamines) has been established to contain antibacterial activities. Studies were conducted to assess the growth inhibiting potential of the complexes synthesized and the ligands against various bacterial strains [sinha 2006].

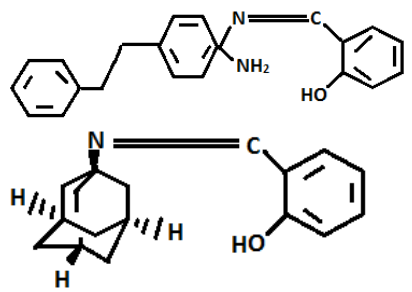
Complexes of Co(II), Ni(II) and Cu(II) with the Schiff base ligands PPNA (Pyrrole-2- carboxaldehyde and m-nitroaniline) (scheme 04) were synthesized and characterized on the basis of the molar conductance, elemental analysis IR, magnetic moment and electronic spectra complexes were also tested for anti fungal activity. [Kumar et al 1998].

Reddy repoted the antibacterial and anthelmentic studies of some complexes which synthesized from $CuCl_2$ and Schiff bases derived from benzaldehydes/ acetophenone with 3-amino 2s-benzofuran carboxamide/ethyl 3-amino 2-benzofurancarboxylate (scheme 05) to yield polymeric complexes of general composition Cu/Cl_2 (L=Schiff base). All the ligands and their metal complexes were found to contain antibacterical activity against S. aureus and anthelmentic activity of the ligands and the complexes against earthworms. [Reddy 2006].

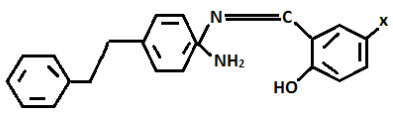


Scheme 04 **scheme 05**

Several schiff bases prepared by the condensation of salicylaldehyde or substituted salicylaldehydes are important class of antimicrobial ligands and this activity increases on complexation. Few of them are discussed here. The treatment of 4-4 diamino dibenzyl with different aldehydes such as salicylaldehyde and substituted salicylaldehydes (scheme 06) have been reported active against E-coli, s-typhii, B.subtilis and s.aureus by Filmwala et al 2007. The antimicrobial activities of schiff bases and their metal complexes have been studied by screening the compounds against micro organism such as E-coli, s-typhii, B.subtilis and s.aureus [Filmwala et al 2007].

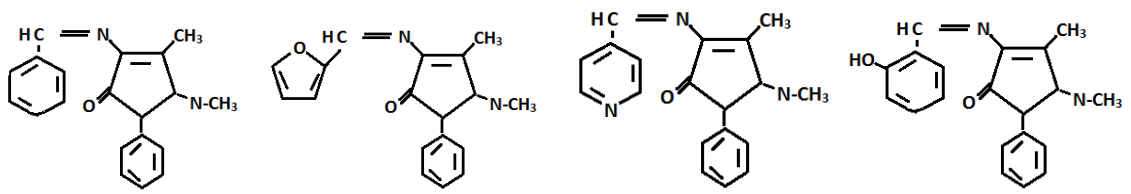


Scheme 06



scheme 07

Another study revealed the preparation of fourteen solid complxes of the lanthanide (III) complexes of the type $[Lu(NO_3)_5(HL)_2]$,Ln=La, Ce, Pr, Nd,Sm,Eu,Gd,Td,Dy,He,Er,Tu,Yb,Lu, $HL=C_{17}H_{21}NO$. in these complexes Schiff base ligands are derived from 1-aminoadamantane and salicyladehyde (scheme 07) . The elemental analysis indicate 1:2 (metal: ligand) stoichiometry for the complexes. The ligand and the complexes were screened for antibacterial activity. It was found that activity against E.coli and B-subtilis has considerably enhanced on complexation [Zhao et al 2008].The complexes of **B**is (cyclopentadienyl) titanium(IV) dichloride with Schiff bases, derived by condensing 4-aminoantipyrine with benzaldehyde(L1), furfuraldehyde (L2),pyridine-4-carboxaidehyde (L3) or salicylaldehyde (L4H),(scheme 08) have been synthesized in anhydrous tetrahydrofuran or dichloromethane. The corresponding complexes were reported to possess antibacterial properties . Sengupta et al 2008.



L1 L2 L3 L4

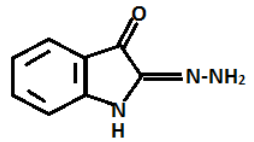
Scheme 08

Similarly the Complexes of dioxouranium (VI) with the schiff base derived from indole-2,3 dione (isatin) and hydrazine (scheme 09) have been synthesized and Various anions such a acetate, lactate nitrate, perchlorate, sulphate and thiocyanate act as secondary ligands by cooridinating to the metal ion. The ligand and some of the complexes were screened for their antibacterical and antifungal activities towards staphylococcus aureans, pseudomonas aeruginosa, E. Coli, Cryptococcus neoformas and Candida albicas [Rajendran et al 2008].

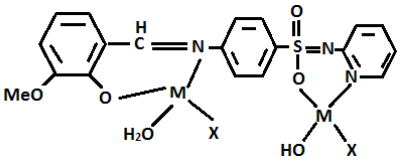
The schiff bases of 2-amino 5-(2-chlorophenyl) 1,3,4 oxadiazoles have been synthesized using aromatic aldehydes (sscheme 10). These compounds were tested against respesentatives of gram possitive (staphylococus aureus) and gram negative bacteria (E. coli and psedomonas aeruginosa), yeast (candida albicans) and mould (As per gillus fumigatus), ciprofloxacin and clotrimazole were used as standard drug for antimicrobial and antifungal activities respectively [shakya et al 2008].

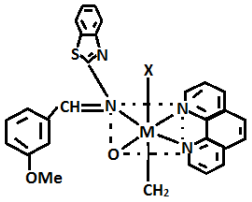
Scheme 10

Some novel mixed ligand complexes of type ML'B (M(II)=Mn(II), Co(II), Ni(II), Cu(II) and Zn(II); HL'=o-vanillidene-2-aminobenzothiazole; B= 1,10-phenanthroline) and Schiff base metal complexes of types (ML2") and (M2L") (11-15) (HL"= *o*-vanillidene-2-amino-N-(2-pyridyl)-benzene sulfonamide) were synthesized and characterized by Neelakanthan et al . 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 [Neelakanthan et al 2008]. In the same manner the Cu(ll),Ni(ll),Zn(ll),Co(ll),Mn(ll) and VO(ll) Schiff base complexes resulting from indole-3-caroxaldehyde (lnd)and amino acids viz, L-alanine(ala), L-phenylalanine (pala) and L-histidine (his) (scheme 11) have been synthesized.The electrochemical properties of Cu(ll) complexes demonstrate distinct quasireversible redox wave accredited to one electron transfer process. The Cu(ll) and Ni(ll) Schiff base complexes were screened for their biocidal activities in vitro on common bacteria [Neelakanthan 2010].



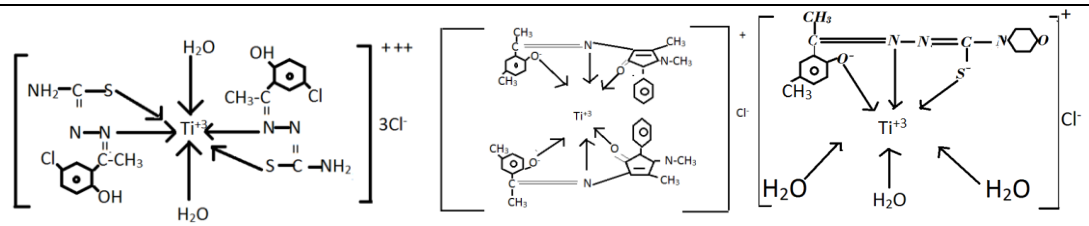
Scheme 09





Scheme 11

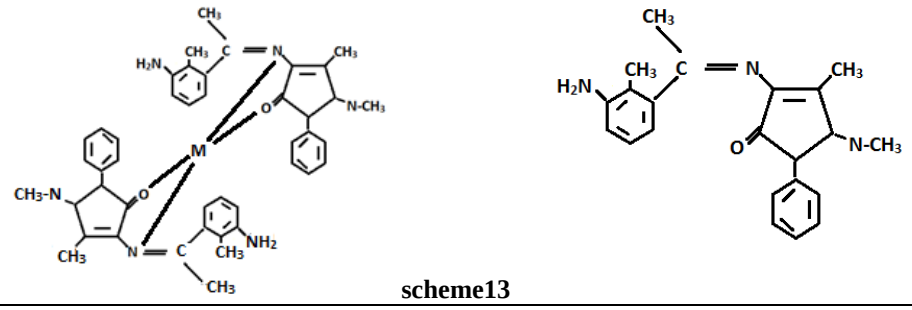
The complexes of Ti (III) synthesized from ligands different ligands like 5-Methyl2-hydroxyacetophenonemorpholine-N-thiohydrazone, 5-Methyl2-hydroxyacetophenone antipyrine, 5-Methyl2-hydroxyacetophenonethiosemicarbazone,2-Hydroxy5 chloro acetophenonemorpholine-N-thiohydrazone and 2-Hydroxy5-chloroacetophenone, thiosemicarbazon) (scheme 12) have been synthesized and screened for their *in vitro* biological activities against bacteria, fungi and yeast. [Nizami et al 2017].



Scheme 12

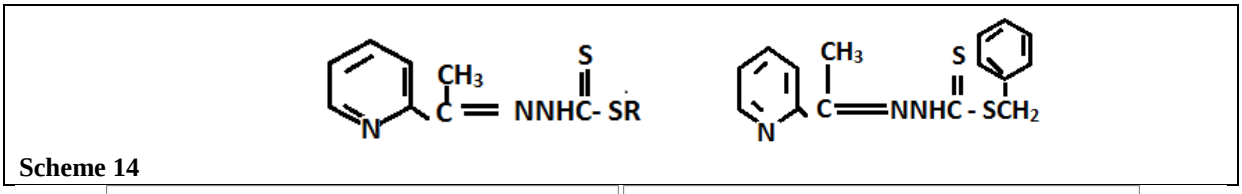
Antibacterial studies of Ni(II) complexes of Heterocyclic Schiff bases have been reported by Saleema. The antibacterical activities of a series of Ni(II) complexes of heterocyclic Schiff bases have been carried out against different bacteria isolated from soil and prawn [Saleema 2005].

Raman et al reported the anti bacterial activities of the bidentate Schiff base ligand derived from 4-aminoantipyrine and o-acetotoluidene and its Cu(II),Co(II),Ni(II) and Zn(II) metal complexes (scheme 13) . Antimicrobial activities of the compounds are tested in vitro against four bacteria and three fungi by the disc diffusion method. The MIC value against the growth of micro-orgnisms is much large for metal chelates than the ligand [Raman et al 2007].

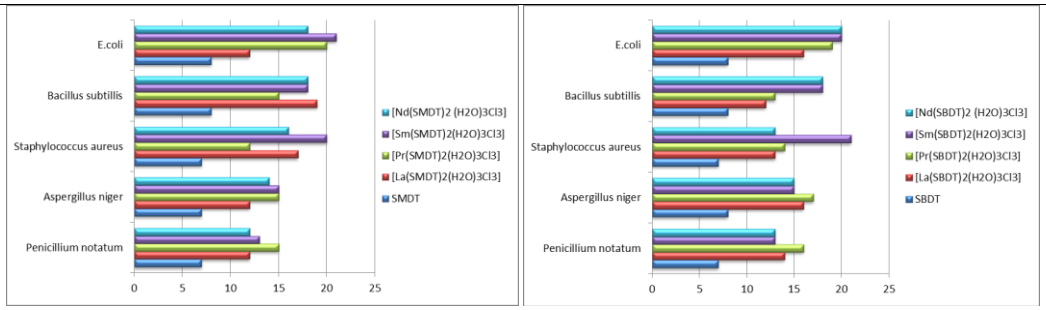


scheme13

In another research the lanthanides complexes have been screened for their biological activity against the bacteria , S.aureus, E.coli and B.subtilis and the fungi Penicillium notatum and Aspergillus niger The La (III), Pr(III), Sm (III) and Nd(III) complexes have been prepared with Schiff bases derived from S- methyl-β-N-(2-pyridyl) methylendithio- Carbazate and S-benzyl-β-N-(2-pyridyl) methylendithiocarbazate (scheme 14). The biological activities were found to be increased with the formation of complexes than ligands [Singh et al 2015].



Scheme 14



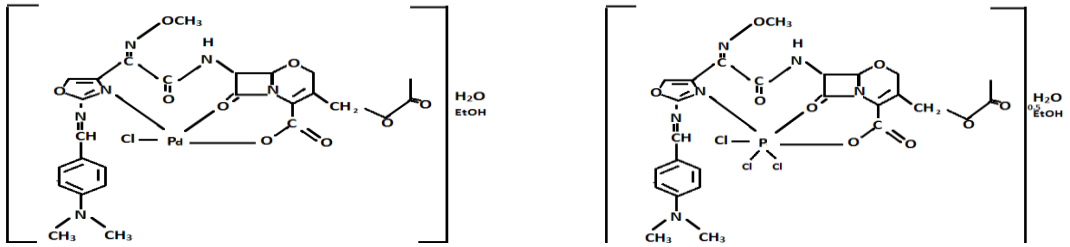
Graph 1. Antimicrobial Activity of Ligand (SMDT) and their Lanthanide Complexes
Graph 2. Antimicrobial Activity of Ligand (SMDT) and their Lanthanide Complexes [Singh et al 2015].

The novel chitosan Schiff base compounds using vanillin and O-vanillin were synthesized and the results of FT-IR studies indicated that chitosan Schiff base complex were effectively formed during blending. From the the thermal stability of the polymer complex was determined from the TGA and DSC studies. The SEM images showed the increased porosity of the chitosan derivatives. [Shashikala et al 2014]

2.2 **Pharmaceutical industry:**

The Schiff base complexes have also been extensively synthesized in pharmaceutical industry due to the remarkable complex formation ability of schiff bases with transition metals and easy synthesis. The syntheses of some Schiff bases from antibiotics are discussed here.

The synthesis of two Schiff base derivatives of cefotaxime antibiotic (CFX) namely[sodium3-(acetoxymethyl)-7-((Z)-2-(methoxyimino)-2-(2-((E)-2–oxoindolin-3-ylide-neamino)thiazol-4-yl)acetamido)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate]. (0.5) Methanol(LI) and [sodium3-(acetoxymethyl)-7-((2Z)-2-(2-(4-dimethylamino) benzylideneamino) thiazol-4-yl)-2-(methoxyimino)acetamido)-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylate] have been done by Abdulhgani et al in 2015. Methanol (LII) from the condensation reaction of the antibiotic with 1H-Indole-2,3-dione(isatin)and -N, N-dimethyl amino benzaldehyde (scheme 15) respectively. Metal complexes of the two Schiff base ligand with Co(II), Ni(II), Cu(II), Cd(II), Pd(II) and Pt(IV) ions were prepared by reacting each ligand with the metal salts in refluxing ethanol.[Abdulghani etal 2015].



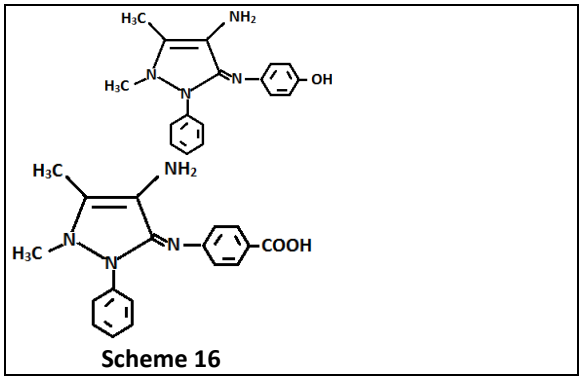
Scheme 15

Another very important study indicated the synthesis of Schiff base complexes from glyoxal, sulphadiazine, sulphaguanidine, diacetylsulphamerazine, sulphamerazine with silicon which are found to have numerous applications in the pharmaceutical industry. The low value of molar conductance reveals nonelectrolytic nature of the complexes [Khan et al 2004].

2.3 Thermodynamics and Electrochemistry:

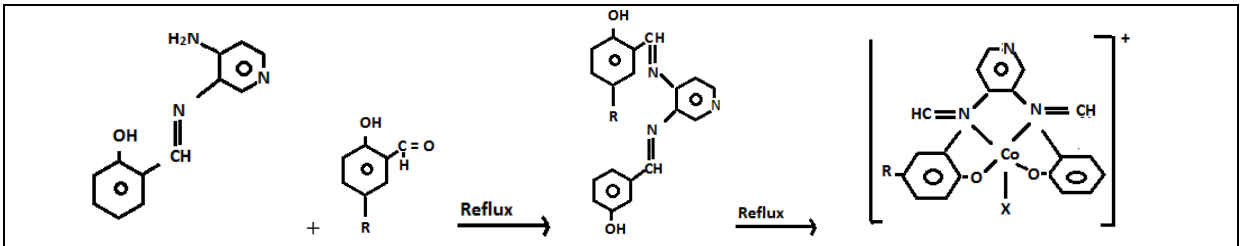
The Schiff base complexes not only played vital role in the antimicrobial studies and pharmaceutical industry but are also synthesized by researchers to study the thermodynamic and electrochemical parameters in a significant quantity. Therefore some of the Schiff bases are discussed here dynamic in electrochemistry and thermodynamics. The complexes of Ni(II) Cu(II) with Schiff bases prepared in an ethanolic medium indicated a distorted octahedral structure for the Cu(II) and Ni(II) complexes and characterized by elemental analysis and molecular weight determination. The IR observations propose that the ligands consist of co-ordinated through OH group. The Biological activity studies have also been presented [GurbaSwaraj & coworkers 2008].Likewise the Cu, Ni, Zn, Co, Mn and UO Schiff base complexes containing indole-3-carboxaldehyde(Ind) and amino acids viz L-alamine (ala)-L-Phenylalanine (pala) and L-histidine (his) have been prepared. The electrochemical properties of Cu complexes exhibit a well difined quasireversible redox wave attributed to one electron transfer process. The Cu and Ni Schiff base complexes were screened for their biodcidal activities in vitro on common bacteria [Neelkanthan et al 2008]. Parameters related to thermal decomposition kineties viz A and Δ s are computed on the basis of thermal decomposition data of the complexes of Sm (III) isothiocyanate with Schiff base ligands viz-4{N-9cinnamalidene) amino} antipyrine (CAAP) and 4 {N-furfural) amino} antipyrine (FFAAP) using three different methods and it was inferred that the values of E are sufficiently high and positive while values of Δ s are negative [Arora et al 1998]. The electrochemical characteristics of a mononuclear Cu(II) complex have been studied and the interaction of Cu complex with DNA was also studied by cyclic voltammetry and fluorescence spectrum [Guo et al 2008] . Another very important study regarding thermodecomposition kinetics of schiff base metal complexes was done by Guo et al. Thermodecomposition kinetics of the complex was calculated under non-isothermal condition. TG and DTG curves point toward the complex decomposition in three steps. The kinetics of step (I) and (3) were calculated by a combination of achar differential and coats-redfen integral methods. The kinetic equations may be expressed as step (1) dα /dt=Ac-E/RT /2(1-)2 [Guo et al 2013].

An important attempt has been made to determine the dissociation constant of synthesized Schiff bases 4-(4-amino-1,5-dimethyl-2-phenyl-1,2-dihydro-pyrazol-3-ylideneamino)-phenol and 4-(4-amino-1,5-dimethyl-2-phenyl-1,2-dihydro-pyrazol-3-ylideneamino)-benzoic acid and metal-ligand stability constants of their complexes with metal ions (Mn^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+}) potentiometrically in 0.1 mol·dm^{-3} KCl and 10% (by volume) ethanol-water mixture and at 298, 308, and 318 K. The stability constants of the complexes was found to be enhanced in the order Mn^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+}. The dissociation process is nonspontaneous, endothermic, and entropically unfavourable, while the formation of the metal complexes was spontaneous, endothermic, and entropically favorable [Bindary et al 2013].



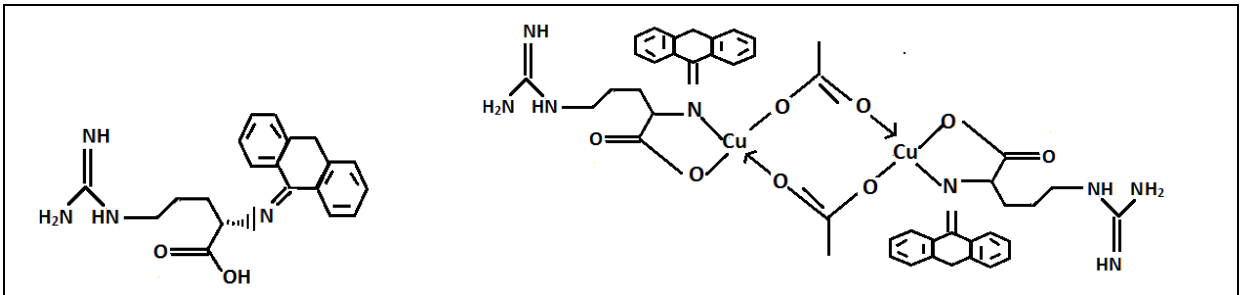
Scheme 16

The Schiff bases resulting from 3,4-diaminopyridine (3,4-DAP) and their novel unsymmetrical Co(III) five coordinate complexes described as [Co(Chel)(L)]ClO4·H2O where (Chel) is the deprotonated form of a series of unsymmetric ligands containing 3,4-diaminopyridine (3,4-DAP) and substituted salicylaldehyde moieties and a new Co(III) six coordinate Co(III) complex, were synthesized. (scheme 16) The fashion of the formation constants of the five coordinate Co(III) Schiff base complexes in the direction of a given phosphine is as tag on: 5-H>5-Br and the formation constants style of these donors are as follow: PBu3>PPh2Me. Additionally the adduct formation of the five coordinate [Co(3,4-Salpyr)(PBu3)] ClO4·H2O, with aromatic amines indicates the following binding trend: Im>2-MeIm>2-EtIm>BzIm. The fashion of the formation constants of Co (III) Schiff base complexes headed for a specified donor according to the phosphine axial ligand is as follow: PBu3>PPh2Me [Asadi et al 2014].



Scheme 16

A new research was conducted for Fe (III)-complexes, Spectrophotometrically complexes followed Beer's law up to definite standards, 6.6×103, 8.0×103dm3mol-1cm-1, respectively, signifying that the ligand HL could be used to identify Co(II) and Ni(II) in such concentrations like Fe (III) complexes. Conductance and thermodynamically used molar ratio technique was to establish the stoichiometry of the complexes synthesized established the formation of 1:1 and 1:2, M:L complexes. The typical thermodynamic parameters viz. ΔG, ΔH and ΔS, for the proton-ligand and the stepwise metal-ligand complexes eluated were analyzed in terms of the electrostatic (eel) and non-electrostatic (crates, c) components. ΔHc was found to be linearly correlated with the acceptor number of the metal ion (ANM), and ΔH el was linearly correlated with the ionic radii of the metal ion. The calculated values for ΔG°, ΔH° and ΔS° concluded that the complexion process processed spontaneously **[**Batouti et al 2015**].** Some Schiff base complexes of Cu (II) resulting from anthracene-9 (10H)- one with (s)-2amino5guandinopentaoic acid (scheme 17) has been synthesized. The redox properties of the ligand and complex were widely investigated by electrochemical method using cyclic voltametry (CV). Cyclic voltametry measurement of Cu (II) complex reveals the quasireversible redox process due to the Cu (II)/ Cu (I) process.



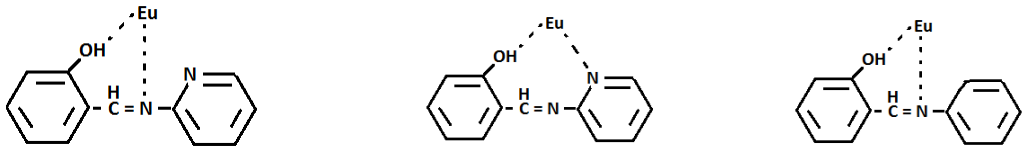
Scheme 17

Structure of Schiff base A9Y5GPA **Structure of Cu (II) A9Y5GPA complex**

Equilibrium based computer models on 8 schiff base complex systems. Viz Coll/Nill/Cull/Znll 2-pyridine carboxaldehyde (A)-L-threonine (thr) and L-ghutamine (gln) (B) systems demonstrate the formation of Schiff base complexes of stoichiometry MAB, MA2B and MA2B2. The Schiff base (AB) binds the metal ion in a tridentate manner. Tetrahedral geometry for CoAB and NiAB Square planar geometry for Cu AB and octahedral geometry for M(AB)2 complexes are indicated[sivasankaan et al 2001]. Proton ligand stability constant of 1-(4-methyl phenyl) 2- (hydroxy5-bro mophenyl) imine (R3) and formation constant of their metal chelates with trivalent La, Ce, Pr, Nd, Sm, Gd, Td,Dy, Yd and Ho have been determined at 25, 35 and 450 and μ=0. 1 M(NaclO4) in 50 : 50 ethanol-water medium by irving-Rossolti method. The log Kll and log K values are used to discuss the effect of substituent and atomic size of the rare earth elements. The thermodynamic parameters for the formation of 1 : 1 and 1 : 2 complexes have been calculate[Naikwade et al 2001].

Non-isothermal degradation and Kinetic parameters of bidentate Schiff base complexes present report about some aspects of non-isothermal kinetic studies of Cu(II),Ni(II),Co(II) and Fe(III) complexes of bidentate Schiff base derived from dehydroacetic acid and ptoluidien [Mane et al 2002]. The electrochemical and EPR spectral properties of some oxovanadium (IV)complexes with Schiff bases (sal-AA) derived from salicylaldehyde and six amino acids viz glycine, L-alanine, L-phe-nylalanine, DL-valine, L-leucine and L-methonine have been studied at a Platinum working electrode in dimethyl sulfoxide (DMSO), Dimethl formamide (DMF) and 50% DMSO aq. (v/v) media contain-ing 0.1M tetrabutyl ammonium perchlorates (TBAP) as supporting electrolyte by means of cyclic voltametry. In DMSO/0.1M TBAP, all these [VO(Sal-AA) H2O] complexes exhibited a totally irreversible anodic peak at + 590 + 10.mv vs SCE at a scan rate 25 mv/s while in 50% DMSO aq. (U/V) 10.1M TBAP media aquarreversible νO2+/ 2+/03/V03+ couple with a format potential E0 = +390 mv Vs SCE was observed. The x-band EPR spectra of these complexes in DMSO at 300 and 77 K were also recorded and their salient features are reported [Prasad etal 2007].

The acid base equilibria and metal ion chelating tendency of 3-(acetophenonhyd- rezone)-6-phenyl pyridazine (AHP) and its p-substituted derivative (XAHP), X = NH2, Cl2 and OMe have been investigated potentiometrically in 75% dioxane water at 298 K and 0.1 M KNO3 (scheme 18). For the same metal ion the order of stability decreases in the sequence NH2AHP>OHAHP>OMeAHP>AHP> ClAHP, which is the same order of decreasing the electron repeling property of the substituent (x) and consequently the basicity of the ligands. The thermodynamic parameters have been evaluated [Saleem et al 2003].



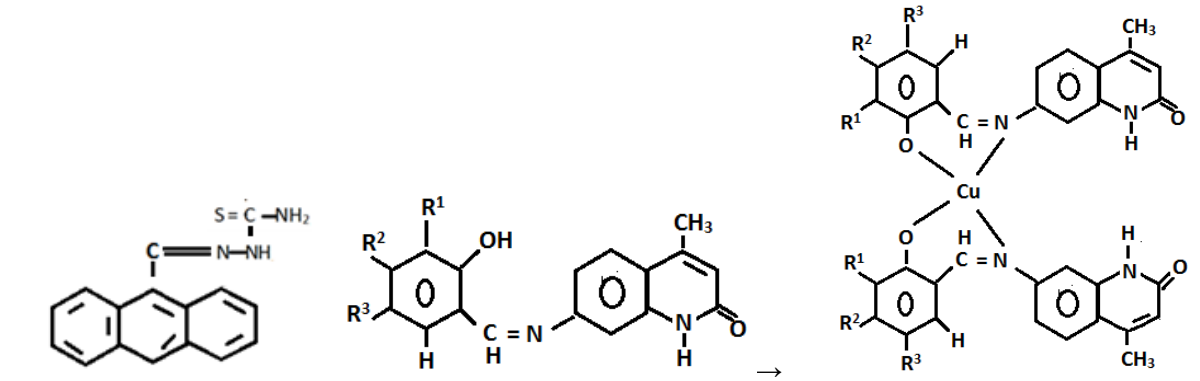
Scheme 18

S2AP S2AP SA

2.4 Anticancer and Antitumor activities:

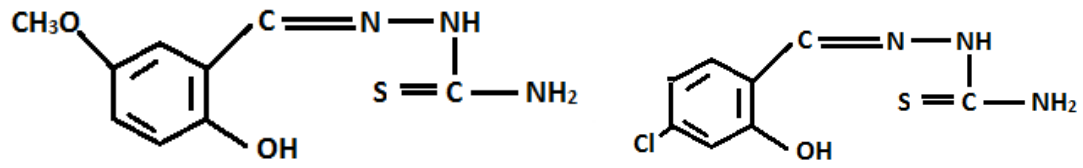
Cancer or malignant neoplasm is a category of diseases in which a cluster of cells demonstrate uncontrolled enlargement, incursion and even sometimes metastasis (De Vita et al., 2005; Thomas and Vinay, 2007). Cancer is the one of the most severe disease of the whole world which causes death of maximum patients. At present the cure of cancer involves surgical treatment and chemotherapy but none of the method is curative successfully, therefore the development of more effective drugs for treating patients with cancer has been a complicated challenge for the researchers in medicinal and medical field over the past 50 years. In the same direction attempts have been made to synthesize various Schiff bases derivatives associated with anticancer and antitumor properties.Thomas in 2002 synthesized the complexes of transition metals having square planar geometry with anthracene -9- carboxaldehydethiosemicarbazone(AacTSC) (scheme 19). The ligand and Cu(II) complex were investigated for antitumor activity. The chelates were found more active in inhibiting mice tumors as compared to ligands. [Thomas et al 2002].

Another investigation for anticancer potential of Schiff base complexes obtained by the condensation of substituted aromatic aldehydes with 7-amino-4-methyl-quinolin-2(1H)-one. All the compounds prepared were investigated for their antimicrobial activities against the fungus, Candida albicans, and against Gram-positive & Gram-negative bacteria. These compounds were found to have tremendous antiCandida activity but were found to be inactive against Staphylococcus aureus and Escherichia coli (scheme 20). These complexes were also screened for their in vitro anticancer potential using the human hepatic carcinoma cell line, Hep-G2. numerous derivatives represented remarkable activity comparable to that of cisplatin [Creavena et al 2010].



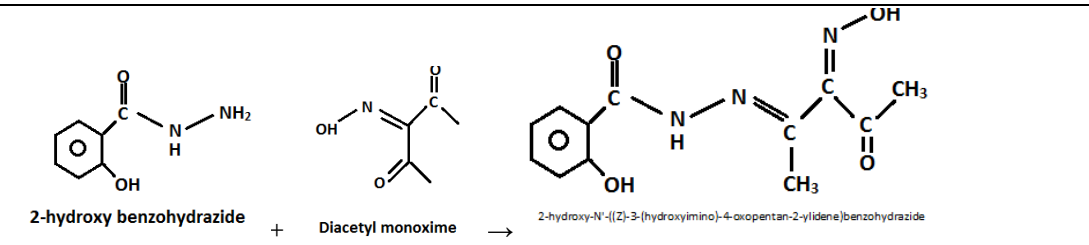
Scheme 19 **scheme 20**

Two oxovanadium(IV) complexes of [VO(msatsc)(phen)], (1) (msatsc = methoxylsalicylaldehyde thiosemicarbazone, phen = phenanthroline) and its new derivative [VO (4-chlorosatsc)(phen)], (2) (4-chlorosatsc = 4-chlorosalicylaldehyde thiosemicarbazone), have been synthesized. Their antitumor effects on BEL-7402, HUH-7, and HepG2 cells were investigated by MTT assay. By cell cycle analysis in BEL-7402 cells, Hoechst 33342 staining, Annexin V-FITC/PI assay, and detection of mitochondrial membrane potential ($\Delta\Psi m$), the antitumor biological mechanism of these two complexes was calculated. These results clearly indicated that the development of cancer cells was prevented considerably, and complexes 1 and 2 largely occurred in BEL-7402 cells G0/G1 cell cycle seize and stimulated apoptosis. Both the complexes have inhibited appreciably the $\Delta\Psi m$, responsible for the depolarization of the mitochondrial membrane. The Complex 2 have been found to exhibit larger antitumor potential than that of complex 1(scheme 21). [Zhang etal 2013]



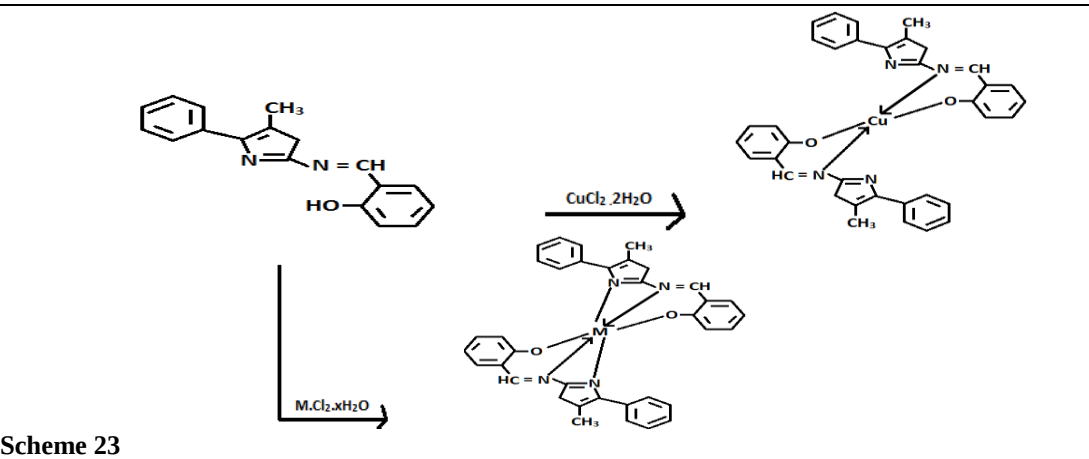
Scheme 21

In a recent study some novel metal (II) complexes derived from 2-hydroxy-N′-((Z)-3-(hydroxyimino)-4-oxopentan-2-ylidene) benzohydrazide ligand (H_2L) were synthesized and characterized (scheme 22). The ESR spectra of the solid copper (II) complexes are characteristic to d^9 configuration and have an axial symmetry type of a $d_{(x^2-y^2)}$ ground state. The ligand and its metal complexes were found to be associated with effective cytotoxicity against enlargement of human liver cancer HepG2 cell lines comparatively from clinically used Sorafenib (Nexavar) [Saad et al 2015].



Scheme 22

The Schiff base ligand((salicyaldehyde with 2-amino-4-phenyl-5-methyl thiazole) and its **complex** of Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II} have been synthesized to study their anticancer potential against different human tumor cell lines like breast cancer MCF-7, liver cancer HepG2, lung carcinoma A549 and colorectal cancer HCT116. Their activity was allowed to compare with the motion of doxorubicin as a reference drug. The Zn^{II} complex found to possess effective inhibition against human TRK in the four cell lines (HepG2, MCF7, A549, HCT116) by the ratio 80, 70, 61 and 64% respectively comparatively with natural cells. Furthermore, the molecular docking into TRK (PDB: 1t46) has also been done for optimization of these compounds as potential TRK inhibitors (scheme 23) [Elzaher et al 2016]

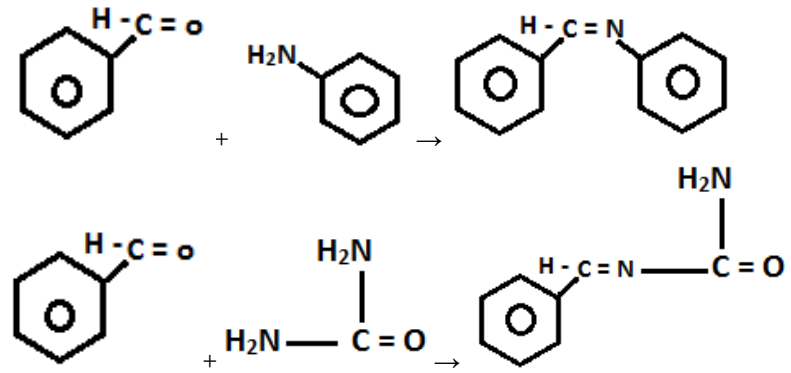


Scheme 23

2.5 Anti environmental pollution properties:

A resin of [5-((E)-1-(ethylimino) ethyl)-4, 7-dimethoxy benzofuran-6-ol] Schiff base (EEDB) was prepared, characterized, and effectively functional in the elimination of Cu (II) ions from aqueous actual samples. The adsorption procedure was moderately rapid and equilibrium was established after concerning 60 min. The optimum initial pH was 8.0 at a metal ion concentration (100 ppm). Under the optimized surroundings, the exclusion of Cu (II) from real samples of tap water was utilized and the elimination efficiency became nearly 85%. The biological activity for Schiff base was also investigated. The results revealed that the effects of Schiff base on serum (alanine amino transferase) ALT resembled with creatinine concentration activities in treated mice and control, at confidence limits 95% [Hassan et al 2013].

Another very important research has been conducted to synthesize Schiff bases by the condensation of primary amine with aldehyde in the absence of organic solvents. The reaction was carried out by natural acid found in different natural products like tamarind and lemon. This reaction is unique due to its inexpensive catalyst, elevated yield of product, easy experimental setting and effortlessly accessible natural products. In this method Benzaldehyde is reacted with Aniline and Urea in the presence of natural acid extracted from tamarind and lemon to give Schiff bases SP-5(Benzylidene aniline) and SP-18 (Benzylidene urea) (scheme 24). These products also exhibit considerably antibacterial, antifungal and antioxidant activities. The synthesis of SP-5 from tamarind and SP-18 from lemon is a innovative eco friendly technique for the production of Schiff base. [Wahab et al 2013].



Scheme 24

Zhang &coworkers in 2017 have synthesized Nanosilica Schiff-base copper(II) complexes (Silica-NMP-Cu) and investigated their antimicrobial activity and toxicity. The results confirmed that, the Silica-NMP-Cu had exceptional antimicrobial activity against four kinds of bacteria, as compared with Kocide with reduced 54.31–64.75% amount of copper. These complexes were not only found to migrate ascending and descending liberally in the plant with the water transportation but also enhance disease resistance by rising the amount of salicylic acid in plants, which is associated with the decreasing the frequency of using copper-based bactericide. The cucumber protection measurement and *Allium cepa*chromoson deviation analysis established that the Silica-NMP-Cu was competent to inhibit the phytotoxicity and the genotoxicity of the copper. The drug release method developed suggested proficient technique to prevent bacteria, as well as decrease the hazard of damage to the plant and the surroundings [Zhang et al 2017].

III. Conclusion

It is evident from the whole discussion that the Schiff bases played a significant role as anticancer, antitumor, antibacterial and antifungal. As well as the complexes of Schiff bases found to be a good medium to carry out electrochemical and thermodynamical analyses. Some complexes were also reported to be active against environmental pollution by many researchers. Therefore it is obvious from above assessment that the Schiff base complexes not only played crucial role in various branch of chemical research in past and in present but also in future Schiff base complexes will have wide scope of research in almost all the braches of chemistry.

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