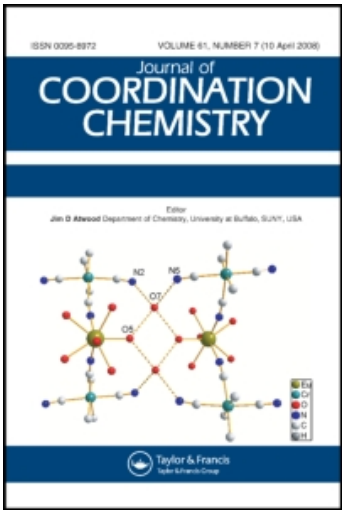

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Transition metal complexes with Schiff-base ligands: 4-aminoantipyrine based derivatives-a review

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Transition metal complexes with Schiff-base ligands: 4-aminoantipyrine based derivatives – a review

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The survey highlights structural properties and biological studies of transition metal complexes derived from 4-aminoantipyrine. The most important results of extensive studies (syntheses, spectral, magnetic, redox, structural characteristics, antimicrobial and DNA cleavage) of the metal complexes with heterocyclic Schiff bases of 4-aminoantipyrine with some aldehydes and oximes are reviewed.

Keywords: 4-Aminoantipyrine; Metal complexes; Synthesis; Physico-chemical characteristics; Biological studies

1. General aspects of heterocyclic ligands

Heterocyclic compounds are widely distributed in nature and essential to many biochemical processes. These compounds are worth attention for many reasons, chief among them are their biological activities; many drugs are heterocycles. Sulfur, oxygen, nitrogen, amino-nitrogen, azomethine nitrogen and alcoholic or phenolic oxygen are some of the donor atoms of interest.

The past few decades have seen the introduction of a number of pharmaceutical compounds which contain five, six, and seven-membered rings such as piperazines, piperidines, imidazoles, benzodiazepines and other heterocycles containing nitrogen, sulfur and oxygen. Compounds containing these heterocycles have important physiological properties ranging from anti-histamine, analgesic, anti-inflammatory, anti-hypertensive and anti-cancer. Such compounds are also used to model important bio-inorganic systems such as metalloproteins and are finding applications as photosensitizers and catalysts.

From early days, the physiological properties of heterocyclic piperazines have generated interest since they are found to exert, even in small dosages, various physiological effects, including accelerated pulse and breathing and hypersensitivity to external stimuli [1]. Some current examples of promising candidates containing a piperazine moiety include the HIV protease inhibitor indinavir [2], a compound that blocks farnesyltransferase activity (anti-cancer) [3], ipsapirone (antidepressant) [4] and

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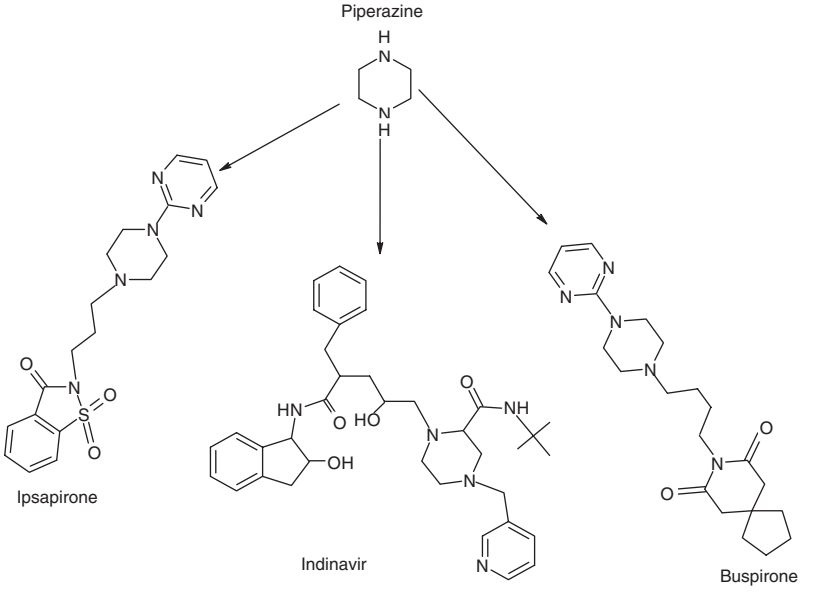
buspirone (anxiolytic drug) [5]. The most thoroughly studied ring system amongst the heterocyclic compounds is pyrimidine. They serve as building units of many valuable chemotherapeutic agents (bleomycine), vitamins (vitamin B_{12}), drugs (hyprotic, antibacterial, antimalarial) and nucleic acids (cytosine and uracil). The piperazine derived compounds of indinavir, ipsapirone and buspirone are given in scheme 1.

Pyrazolone (N-heterocyclic compound) is an active moiety as a pharmaceutical ingredient, especially in nonsteroidal anti-inflammatory agents used in the treatment of arthritis and other musculoskeletal and joint disorders. Earlier work reported that some drugs showed increased activity when administered as metal chelates rather than as organic compounds. The coordinating behavior of 4-aminoantipyrine has been modified into a flexible ligand system by condensation with a variety of reagents like aldehyde, ketone etc. [6–10].

2. Characteristics of pyrazolone

Pyrazolone sometimes refers to nonsteroidal anti-inflammatory agents. Pyrazolone class NSAID (nonsteroidal anti-inflammatory drug) includes phenylbutazone, oxyphenbutazone, dipyrone, and ramifenazone which are in scheme 2. These ligands contain pyrazolone and antipyrine in their structures which have the heteroatoms in the ring. These heteroatoms induce the biological activity of nonsteroidal anti-inflammatory agents.

Antipyrine has been used as an antipyretic, but replaced due to the possibility of agranulocytosis side-effect. Lactams have big demand in artificial fiber industry.



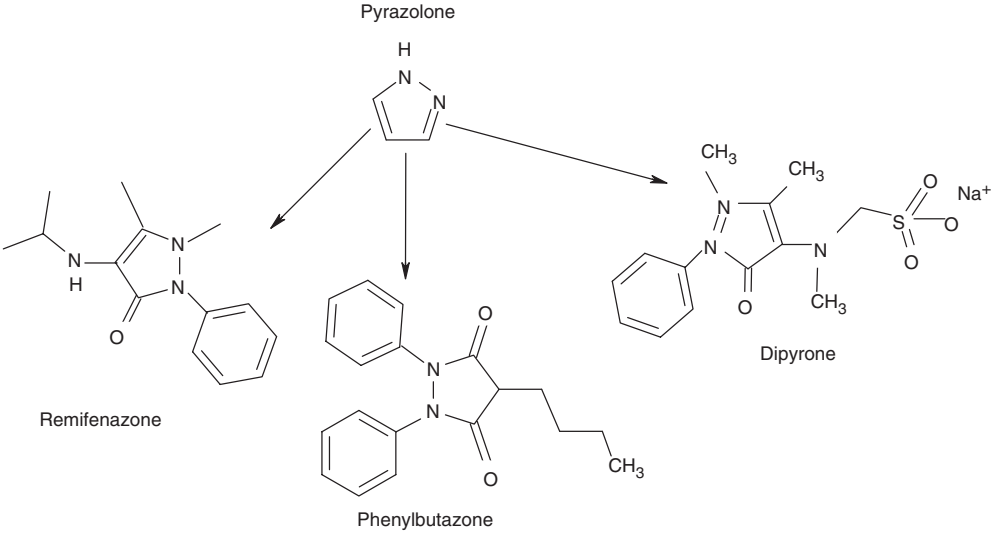
Scheme 1. Piperazine derived compounds.

Pyrazolone derivatives, as lactam structure related compounds, are also widely used in preparing dyes and pigments. Pyrazolines are five-membered nitrogen containing heterocyclic compounds. Various procedures have been developed for their synthesis. Formation of pyrazolines has been reported [11–15] by the action of nucleophiles like hydrazine hydrate or phenylhydrazine etc. Pyrazolines have been used in textiles, killing house-flies [16], antifungicidal [17], analgesic [18] and antimicrobial agents [19, 20]. Many medicines contain a pyrazole ring system. Pyrazoline derivatives have been found to be effective insecticides, pharmaceuticals and fungicidal agents.

3. Coordination behavior of 4-aminoantipyrine (AAP)

As early as 1884, Knorr discovered the antipyretic (temperature reducing) action of a pyrazole derivative in humans, and due to its antipyretic property he named the compound "Antipyrine." Transition metal complexes of pyrazolone derivatives are of great interest due to their biological activities, especially pyrazolone Schiff-base derivatives. Among the pyrazolone derivatives, 4-aminoantipyrine forms a variety of Schiff bases with aldehydes/ketones, and they are reported to be superior reagents in biological, pharmacological, clinical and analytical applications [21]. 4-Aminoantipyrine has an N-phenyl group and a –CH group on either side of a polar carbonyl group, thus resembling N-substituted amides. Coordination chemists, medicinal chemists and analytical chemists have extensively studied 4-aminoantipyrine. The carbonyl group in 4-aminoantipyrine is a potential donor due to the large dipole moment (5.48 D) and strong basic character.

Three modes of coordination must be considered for the system, unidentate with bonding through either oxygen or the amino nitrogen or chelation utilizing both



Scheme 2. Pyrazolone class nonsteroidal anti-inflammatory compounds.

these donors. The majority of the Schiff bases of 4-aminoantipyrine derivatives are obtained in good yield by condensation of aqueous or alcoholic solution [22, 23]. Depending upon the form (neutral, protonated) of the ligand precursor, it is possible to obtain either neutral or protonated forms of the ligands. Since 4-aminoantipyrine has an additional potential coordination site in the amino nitrogen, it was considered worthwhile to study the complexes of this ligand.

4. Complexes derived from 4-aminoantipyrine

Guru and Rao [24] prepared zinc complexes of 4-aminoantipyrine. Gopalakrishnan and Patel [25] carried out the physico-chemical studies on antipyrine complexes of $CoCl_2$, $CoBr_2$, $CuCl_2$, and $CuBr_2$ of the type $MX_2 \cdot 2AAP$. Both electrical conductance and cryoscopic determination of molecular weight in nitrobenzene showed them to be monomeric non-electrolytes.

Bose and Patel [26] prepared the Cu(II) nitrate and bromide complexes of 4-dimethylaminoantipyrine and characterized them by spectral studies. Prabhakaran and Patel [27] prepared antipyrine complexes of Fe(III) chloride and thiocyanate. The lowering value of the C=O stretch in IR spectra suggest coordination through the carbonyl oxygen to Fe(III).

Mixed ligand complexes of thorium(IV) derived from 4[N-(2-hydroxy-1-naphthalidene)amino]antipyrinesemicarbazone (HNAAPS) or 4[N-(cinnamalidene)-amino]antipyrinesemicarbazone (CAAPS) as primary ligand and diphenyl sulfoxide (DPSO) as secondary ligand with the general composition $ThX_4 \cdot n(L) \cdot DPSO$ ($n = 1$, X = Cl, Br, NCS or NO_3; $n = 2$, X = I or ClO_4, L = HNAAPS or CAAPS) were synthesized and characterized through elemental analysis, molar conductance, IR and thermogravimetric analysis [28].

4.1. *Condensation of 4-aminoantipyrine amino group*

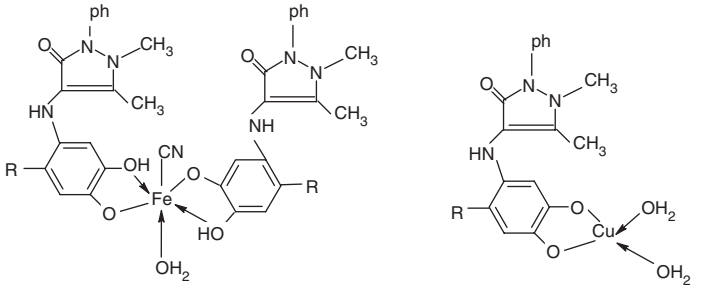
The largest group of Schiff-base metal complexes which have been synthesized and characterized represent complexes with 4-aminoantipyrine and its derivatives with some aldehyde, ketone etc. With respect to the applied methods and synthetic conditions of metal complexes bearing these ligands, practically all the complexes were obtained by the simple non-template method, i.e. by the reaction of ready-made ligands and metal salts, mainly in warm alcoholic solution under air.

Lanthanide perchlorate complexes with 4-N-(2-hydroxy-1-naphthalidene)aminoantipyrine, $[Ln(L)_2ClO_4]$ [where Ln = La(III), Pr(III), Nd(III) or Sm(III)] and $[Ln(HL)_4](ClO_4)_3$ [where Ln = Gd(III), Tb(III), Dy(III) or Ho(III)], have been synthesized and characterized [29]. Ni(II) complexes of 4-N-(2-hydroxy-1-naphthalidene) aminoantipyrine (**1**) and 4-N-(2-hydroxy-1-benzalidene)aminoantipyrine (**2**) were prepared by stoichiometric amounts of hot ethanolic solution of $NiCl_2 \cdot 6H_2O$ and the ligand and sodium acetate in 1 : 1 ratio. The thermochromism in crystalline **1** and **2** has been attributed to dehydration of the complexes [30].

Kuncheria *et al*. [31] synthesized ten new complexes of thorium(IV) nitrate with Schiff bases derived from 4-aminoantipyrine (4AAP) and carbonyl compounds such as

benzaldehyde, 2-nitrobenzaldehyde, 3-nitrobenzaldehyde, 4-methylbenzaldehyde 4-N, N-dimethylaminobenzaldehyde, 2-hydroxybenzaldehyde, 2-hydroxy-acetophenone, acetylacetone, benzoylacetone and 2-hydroxy-1-naphthaldehyde. These complexes have been characterized by elemental analyses, molecular weight determination, conduction and spectral studies. Mn(II), Co(II) and Ni(II) complexes with tridentate Schiff bases derived from 4-aminoantipyrine and different aldehydes (2-hydroxy-1-naphthaldehyde and 2, 4-dihydroxybenzaldehyde) were isolated. For all complexes, spectroscopic results suggested an octahedral geometry [32]. Savant and Ramamurthy [33] studied antipyrine complexes of Ti(II), Zr(II), Th(IV) and U(IV) perchlorates. They are stable at room temperature and decomposed exothermally at 300°C. Spectral studies indicated the bonding of metal to ligand through carbonyl oxygen. Nair *et al*. synthesized new lanthanide nitrate complexes of the Schiff base derived from 4-aminoantipyrine and 2-hydroxybenzaldehyde [34, 35] *viz*. 4[N(2-hydroxybenzylidene)amino]antipyrine. Gadre *et al*. [36] reported isolation and structure elucidation of complexes of the Schiff-base ligands, salicylidene-4-aminoantipyrine and acetylaceto-4-aminoantipyrine with UO_2^{2+} and Ln^{3+}, respectively. In 1986, Agarwal *et al*. [37] synthesized a new Schiff base by condensing 4[N(benzylidene)amino]antipyrine with semicarbazide. The semicarbazide forms an azomethine group with the cyclic carbonyl present in the 4-aminoantipyrine [38]. Ismail *et al*. [39] synthesized copper complexes derived by condensation of 4-aminoantipyrine with furfuraldehyde and the corresponding thiophenealdehyde, 4-furfurylidene-aminoantipyrine and 4[N(2-thienylmethylidene) amino]antipyrine. Mohamed *et al*. [40] synthesized Fe(III) and Cu(II) complexes derived from catecholamine and 4-aminoantipyrine. These were characterized by IR, UV-Vis, magnetic and thermal studies which indicated that Fe(III) forms 1 : 2 (M : catecholamines) chelates while Cu(II) forms 1 : 1 chelates. Magnetic moment measurements reveal the presence of Fe(III) chelates in octahedral geometry while the Cu(II) chelates are square-planar; the structures of the complexes are given in scheme 3.

Agarwal *et al*. [41] synthesized some high coordinated complexes of thorium(IV) and dioxouranium(VI) derived from 4[N(2-hydroxy-1-naphthalidene)amino]antipyrine and thiosemicarbazone. All compounds were characterized by analytical, molar mass, molar conductance and infrared studies. Thermal stabilities of these complexes were investigated through thermogravimetric analysis. Issaadi *et al*. [42] synthesized an N_2O_3 type Schiff base and its complexes with Cu(II), Co(II), Zn(II) and Cd(II), characterized by spectroscopic determinations and cyclic voltammetry. The spectral techniques indicated that the Cu(II) and Cd(II) complexes are mononuclear while the Co(II) and Zn(II) complexes appeared to be binuclear.



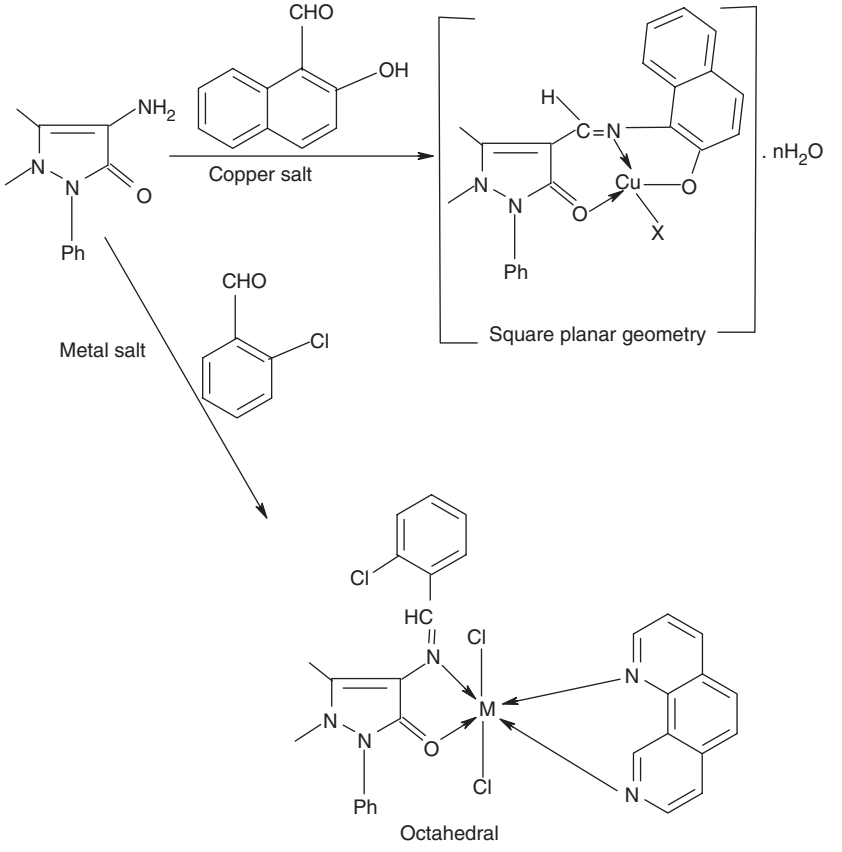
Scheme 3. Octahedral and square-planar geomentry of the complexes with 1:2 and 1:1 ratio.

Iron(III) complexes of 4[N(antipyrylmethylidene)amino]antipyrine with counter ions, such as perchlorate, nitrate, thiocyanate, chloride and bromide, have been prepared by Linert *et al*. [43] and characterized by elemental analyses, electrical conductance in non-aqueous solvents, IR and electronic spectra, magnetic susceptibility measurements, as well as by thermogravimetric analysis. Kinetic parameters like activation energy, pre-exponential factor and entropy of activation were also computed.

Issa *et al*. [44] synthesized five Schiff bases derived from 4-amino antipyrine and benzaldehyde derivatives; their UV–Vis, IR, ^{1}H NMR and fluorescence spectra were investigated, supported by MO calculations using an atom superposition and electron delocalization molecular orbital theory. The square planar and octahedral geometry of the 4-aminoantipyrine derived metal complexes are given in scheme 4 [22, 44].

Donia and Ebeid [45] synthesized Ni(II) complexes using ligands such as 4[N (2-hydroxy-1-naphthylidene)amino]antipyrine and 4[N(salicylidene)amino]antipyrine. These complexes were studied using differential thermal analysis, electronic and IR spectroscopy, X-ray powder diffraction and electrical conductivity. Thermochromism in these complexes has been attributed to dehydration.

Liang *et al*. [46] synthesized Cu(II) complexes of the Schiff base derived from picolinaldehyde N-oxide and 4-aminoantipyridine. These were characterized



Scheme 4. Octahedral and square-planar geometry derived from different aldehydes.

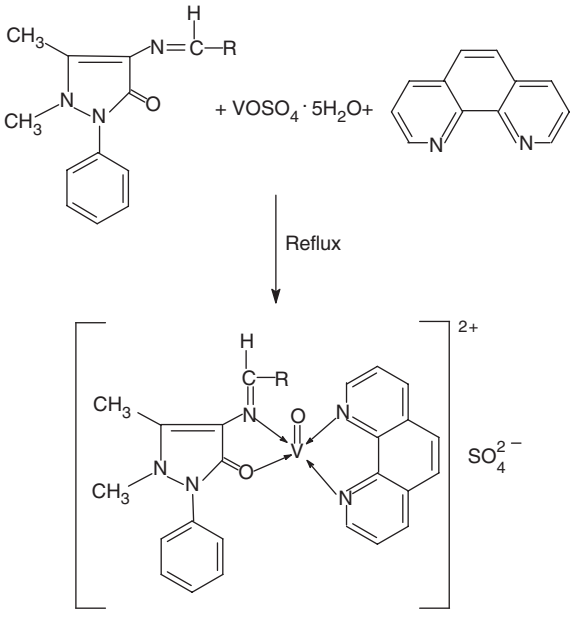
by elemental analysis, IR, ^{1}H NMR and single crystal X-ray crystallographic determination. Alaudeen *et al.* [47] reported transition metal chelates of Mn(II), Cr(II), Fe(III), Co(III), Zn(II) and Cd(II) with 4-aminoantipyrine, thiosemicarbazide and 2-aminobenzothiazole. Molecular modeling studies revealed energy minimization and the study was repeated several times to find the global minimum value. Ravindran [48] reported iron(III) complexes derived from 4-aminoantipyrine and acetylacetone, characterized by elemental analyses, conductance measurements, IR, UV-Vis, and Mossbauer studies. The spectral techniques suggested the complex has octahedral geometry around iron(III).

Agarwal *et al.* [49] synthesized lanthanide(III) complexes derived from 4-aminoantipyrine, 4-methoxybenzaldehyde and thiosemicarbazone, condensing the carbonyl group of the 4-amino antipyrine with thiosemicarbazone. These were characterized by magnetic, spectral and thermal techniques. Agarwal *et al.* [50] synthesized copper(II) complexes of thiosemicarbazones of Schiff bases derived from 4-aminoantipyrine and some aromatic aldehydes, which were characterized through elemental analysis, molecular weight, electrical conductance, infrared, electronic spectra and magnetic susceptibilities and were screened for antibacterial and antifungal properties.

Sinha *et al.* [51] synthesized Pd(II) and Ag(II) complexes derived from 4-aminoantipyrine and imidazole. These complexes were characterized by UV-Vis, IR and ^{1}H NMR spectral studies. Rosu *et al.* [52] synthesized Cu(II) complexes derived from 4-aminoantipyrine and salicylaldehyde, which were characterized by ^{1}H NMR, UV-Vis, IR and ESR spectroscopy. Determinations of the antimicrobial activity of the ligands and the complexes were carried out against some bacteria. Complexes of uranyl(VI) nitrate with functional Schiff bases derived from acetylacetone, salicylaldehyde and 2-hydroxy-1-napthaldehyde with 4-aminoantipyrine were synthesized from neutral or alkaline reaction media and their spectra-structure correlation obtained. The ligands behave differently at different pH of the reaction solution [53]. Issa [54] *et al.* prepared five new Schiff bases derived from 4-aminoantipyrine with benzaldehyde, *o*-hydroxybenzaldehyde, *p*-methoxybenzaldehyde, *p*-hydroxybenzaldehyde and 2-hydroxy-1-naphthaldehyde, and the UV-vis, IR, ^{1}H NMR and fluorescence spectra were investigated.

Three oxovanadium(IV) Schiff-base complexes having the formula VO(Phen)(L)]SO_4 (where L = 4[(benzylidene)amino]antipyrine, [(cinnamalidene)amino]antipyrine and 4[(2-chlorobenzylidene)amino]antipyrine) were designed using benzaldehyde/cinnamaldehyde/2-chlorobenzaldehyde with 4-aminoantipyrine, 1,10-phenanthroline, and vanadyl sulphate in the 1 : 1 : 1 molar ratio. Microanalytical and spectral techniques were used to confirm the structures. Electronic spectral studies suggest square-pyramidal geometry around vanadium [55]. The geometry of the 4-aminoantipyrine vanadyl complexes are shown in scheme 5.

Nair and Thomas [56] reported oxovanadium complexes derived from 4-aminoantipyrine and *p*-chlorophenol by diazotization and coupling and characterized them by spectral techniques. All the complexes were monomeric and neutral with square-pyramidal geometry. Nair and Mathew [57, 58] reported mercury(II)/dioxotungston chelates of azo dyes derived from 4-aminoantipyrine and *p*-cresol/*p*-cholorophenol/*p*-nitrophenol. These complexes were screened against some bacteria for antibacterial activity. Nair *et al.* [59] synthesized Cu(II) complexes derived from 4-aminoantipyrine and *p*-cresol/*p*-chlorophenol by diazotization and coupling. All the complexes have square-planar geometry. West *et al.* [60] synthesized iron(III), cobalt(II/III), nickel(II),



Scheme 5. The square-pyramidal geometry of the vanadyl complexes.

copper(II) and zinc(II) complexes derived from 2-formylpyridine, N-antipyrinyl and thiosemicarbazone. Ligand field parameters were calculated and the proposed stereochemistry is based on various physical and spectral methods. Bhattacharaya *et al*. [61] prepared adducts of some aryltinhalides with antipyrine. The IR data of this adduct indicated coordination through the carbonyl oxygen of the ligand.

Bailey and Peterson [62] observed that 4-aminoantipyrine was a monodentate ligand bonding through nitrogen in complexes of Cu(II), Co(II) and Ni(II) only when bromide anion was coordinated to the metal. This may be due to the greater ability of bromide to accept electrons from the metal ion *via* back bonding, thereby reducing the electron density on the metal. This effect could be counteracted by donation from nitrogen rather than from oxygen. A large number of compounds of antipyrine have been shown to be unidentate; oxygen coordination is confirmed from IR spectral studies [63–65].

A new series of transition metal complexes of Cu(II), Ni(II), Co(II), Mn(II), Zn(II), VO(IV), Hg(II) and Cd(II) have been synthesized from the Schiff base (L) derived from 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and *o*-phenylenediamine. Structural features were obtained from their elemental analyses, magnetic susceptibility, molar conductance and spectral studies. The data show that these complexes have ML composition [66].

Iron(III) complexes [67] of the Schiff base 4-N-(4′-antipyrylmethylidene)aminoantipyrine (AA) with counterions such as perchlorate, nitrate, thiocyanate, chloride and bromide have been prepared and characterized by elemental analyses, electrical conductance in non-aqueous solvents, IR and electronic spectra, magnetic susceptibility measurements, as well as by thermogravimetric analysis. The complexes have formulae $[Fe(AA)_2(ClO_4)](ClO_4)_2$, $[Fe(AA)_2X_2]X$ ($X = NO_3^-$ or Br^-) and $[Fe(AA)X_3]$ ($X = SCN^-$ or Cl^-). A high spin octahedral geometry is assigned to the iron(III) in all these complexes.

The chelates of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) with 4-formyloxime-1,3-diphenyl-2-pyrazolin-5-one (FDPPZ) derived from 4-formyl-1,3-diphenyl-2-pyrazolin-5-one and hydroxylamine [68] were characterized by elemental analysis, conductivity, magnetic measurements and spectral studies. The IR spectra suggest bidentate ligand. All the chelates except Cr(III), Fe(III) and VO(IV) have composition $M(FDPPZ)\cdot H_2O$, while Cr(III) and Fe(III) chelates were $M(FDPPZ)_3$. The ligand field parameters for VO(IV), Cr(III), Co(II) and Ni(II) chelates were calculated. Infrared spectra of 4AAP and its duplexes are quite complex due to the presence of numerous functional groups in the molecule [69].

4.2. *Condensation of 4-aminoantipyrine carbonyl group*

The carbonyl group of 4-aminoantipyrine was also condensed by primary amino groups. Chakaraborti [70] synthesized ten new nickel(II) coordination compounds of 4-[N-(2-hydroxy-1-naphthalidene)aminoantipyrine thiosemicarbazone and 4-[N-(cinnamalidene)aminoantipyrine thiosemicarbazone of general formula $NiX_2\cdot L\cdot H_2O$ ($X = Cl^-$, NO_3^-, NCS^- or CH_3COO^-) or $Ni(ClO_4)_2\cdot 2L$. The complexes were characterized on the basis of elemental analyses, molecular weight, conductivity, magnetic moment, IR and electronic spectral data. The coordination number of Ni^{2+} in these complexes is presumed to be six with octahedral geometry. In all the complexes both thiosemicarbazones were neutral tridentate (N, N, S) ligands. Thermogravimetric data of the Ni complex indicated that the complex is stable to *ca* 140°C, indicating the complex is non-hygroscopic. Reaction of Cu(II) salts with 4-[N-(2-hydroxy-1-naphthalidene)aminoantipyrine thiosemicarbazone (HNAAPT) resulted in formation of $CuX_2(HNAAPT)\cdot H_2O$ ($X = Cl^-, Br^-, NO_3$, NCS^- or CH_3COO^-). Characterizations of these complexes were made on the basis of elemental analysis, molecular weight, magnetic moment, conductivity measurements, IR and UV-vis. Thermal properties of these complexes were also investigated [71].

Neutral tetradentate complexes of Cu(II), Ni(II), Co(II), Mn(II), Zn(II) and VO(IV) were synthesized [72] using Schiff bases derived from 2-aminophenol/2-aminothiophenol and 4-(N-iminopentane-2-one)aminoantipyrine in ethanol and characterized by microanalytical data, IR, UV-vis, ^1H NMR and ESR spectra. The IR and UV-vis spectra suggest that all the complexes have square-planar geometry except vanadyl and manganese complexes which show square-pyramidal and octahedral geometries, respectively. The redox behavior of copper and vanadyl complexes has been studied by CV and ESR spectra of copper and vanadyl complexes were also discussed. Antimicrobial activity of the Schiff base and complexes have been extensively studied on some microorganisms.

In our laboratory we [73] synthesized a few metal complexes of 4-aminoantipyrine ML, where M = Cu(II), Ni(II), Co(II), Zn(II) and VO(II) and the manganese complexes $MnL\cdot 2H_2O$ (L = neutral tetradentate ligand derived from acetoacetanilido-4-aminoantipyrine and 2-aminophenol/2-aminothiophenol). Microanalytical data, IR, UV-vis, ^1H NMR and ESR spectral techniques suggest the complexes have square-planar geometry except for VO(IV) and Mn(II) complexes which have square-pyramidal and octahedral geometry. The antimicrobial activity of the complexes was tested against some bacteria.

Cu(II) complexes have been synthesized from the Schiff base derived from salicylidene-4-aminoantipyrine and aniline/*p*-chloroaniline, *p*-methylaniline/*p*-nitroaniline. The structural features have been determined from microanalysis and spectra, which show that all the complexes were square planar. The antimicrobial activity and powder XRD pattern of all the complexes were also reported [74]. A tetraaza macrocyclic Schiff base synthesized from 1,2-(diimino-4-antipyrinyl)-1,2-diphenylethane and *o*-phenylenediamine was a tetradentate ligand forming cationic complexes with Cu(II), Ni(II), Co(II) and VO(IV) salts in ethanol. All the synthesized complexes were characterized by elemental analysis, IR, UV-vis, ^{1}H NMR, ESR and mass spectral techniques. The IR and UV-vis spectra suggested that all $[ML]Cl_2$ complexes were square planar, whereas $[CuL(Y)_2]Cl_2$ were octahedral (where Y = pyridine, imidazole or triphenylphosphine). The $[VOL]SO_4$ complex was square pyramidal. The ESR spectra of copper and vanadyl complexes were recorded and their M.O. coefficients calculated [75].

Reaction of CoX_2 ($X = Cl^-$, NO_3^-, NCS^- or CH_3COO^- or ClO_4^-) with 4-[N-(benzalidene)aminoantipyrine thiosemicarbazone and 4-[N-(2-hydroxybenzalidene)aminoantipyrine thiosemicarbazone yielded complexes of general formula $CoX_2(L)H_2O$ or $Co(ClO_4)_2 \cdot 2L$. All the complexes were six coordinate according to magnetic and electronic spectral measurements. The IR data of the complexes indicated both thiosemicarbazones were neutral tridentate(N, N, S) ligands [76].

5. Spectroscopy of pyrazolone and complexes

5.1. *Electronic absorption spectra*

The spectra of numerous transition metal complexes containing different Schiff-base ligands have been described in the literature [77, 78]. The obtained spectra display electronic transitions characteristic of ligands and metal ions in coordination. These spectra are sensitive to the type of ligand and has proved to be useful in identification of particular complex species. The electronic spectra of 4-aminoantipyrine derived ligands show four main absorptions in ethanol between 200–400 nm. The first (210–234 nm) and second (240–281 nm) are assigned to π–π^* transitions of the aromatic ring. The band at 301–334 nm involves π–π^* transitions of the C=O and C=N groups; the longer wavelength band (325–396 nm) can be assigned to an intramolecular charge transfer, originating from the 4-aminoantipyrine ring to the C=O as a sink. This was confirmed by determining the energy of the CT band from λ_{max} values using the relation

$$E_{CT} = 1241.6/\lambda_{max}CT$$

and comparing the values thus obtained with those calculated from the Briegleg relation [79]

$$E_{CT} = I_p - (E_A + C)$$

I_P = ionization potential of the donor part; E_A = electron affinity

The oscillator strength (f) of the CT band was also determined from the relation [80].

$$f = 4.6 \times 10^{-9} \varepsilon_{max} \Delta\nu_{1/2}$$

Numerous authors have studied changes in spectra upon the addition of metal ions. Some also interpretated the d-d transitions of such metal complexes. The d-d transitions in the Ni(II) complexes of HNAAP show bands of relatively low intensity around 16529 cm^{-1} and 23810 cm^{-1}, assigned to $^3T_{1g}(F) \leftarrow {}^3A_{2g}(F)$ and $^3T_{1g}(P) \leftarrow {}^3A_{2g}(F)$ transitions, respectively, for octahedral geometry.

The spectra of another Ni(II) complex [75] show three predominant peaks, two INCT bands and the remaining one at 15823 cm^{-1} due to $^1A_{1g} \leftarrow {}^1B_{1g}$. This d-d transition strongly indicates square-planar geometry. The observed zero magnetic moment confirmed square-planar environment for the Ni(II) macrocyclic complex [81].

The electronic spectra of the chromium complex [82] of 4-formyloxime-1,3-diphenyl-2-pyrazolin-5-one (FDPPZ) show bands at 18116, 21367 and 27397 cm^{-1}, assigned to $^4B_{1g} \rightarrow {}^4E_g$, $^4B_{1g} \rightarrow {}^4B_{2g}$ and $^4B_{1g} \rightarrow {}^4A_{2g}$, respectively [83]. An attempt was made to calculate the absolute ligand field parameters [84] DT, Dq^{xy} and DQ^z. The value of the ratio $DT/DQ = 0.09524$ suggest that [85] $Cr(FDPPZ)_3$ is moderately distorted. The spectrum of $Mn(FDPPZ)_2 \cdot H_2O$ shows bands at 17241 and 21505 cm^{-1}, attributed to $^6A_{1g} \rightarrow {}^4T_{1g}(G)$ and $^6A_{1g} \rightarrow {}^4T_{1g}(Eg)$, respectively, in an octahedral field.

The electronic spectra of Cu(II) complexes consist of a broad band at 16200 cm^{-1} of medium intensity in the visible region identified as a d-d transition. The ligand field parameter was estimated from the equation suggested by Lever *et al.* These data are in agreement with those reported for other D_{4h} complexes.

The octahedral Co(II) high spin complex absorbs at 9328 and 17699 cm^{-1}, assigned as $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ in an octahedral geometry. The observed transition energies were used to calculate 10 Dq, B, β. The electronic spectra of VO(IV) complexes show bands around 19608 and 13315 cm^{-1}, assigned to $^2B_2 \rightarrow {}^2A_1$ and $^2B_2 \rightarrow {}^2E$. Kharodawala *et al.* [82] showed three bands at 9871, 21834 and 28328 cm^{-1} assigned to $b_2 \rightarrow e$, $b_2 \rightarrow b_1$ and $b_2 \rightarrow a$ transitions. Making use of these transition energy parameters such as DT, DQ^{xy}, DQ^z have been evaluated.

The electronic spectrum of $Fe(FDPPZ)_3$ shows bands at 17391, 19230 and 22123 cm^{-1}, assigned to transition $^6A_{1g} \rightarrow {}^4T_{1g}$, $^6A_{1g} \rightarrow {}^4T_{2g}$, E, respectively.

5.2. *IR spectroscopy*

Practically all the ligands and their complexes of 4-aminoantipyrine have been characterized in detail by recording their IR spectra. A common feature of all these spectra is absorptions in the medium range *i.e.* 1700 cm^{-1} and 1600 cm^{-1}, ascribed to ν(C=O) and ν(C=N). The IR spectra of 4-aminoantipyrine exhibit two medium intensity bands around 3174–3038 cm^{-1} and 3087–3036 cm^{-1} corresponding to asymmetric and symmetric vibration of the aromatic C–H group. All the compounds show an intense band at 1648 cm^{-1} corresponding to C=O group [54].

The metal complexes derived from 4-aminoantipyrine have a very strong absorption band near 1660 cm^{-1} and a weak absorption band near 1625 cm^{-1} assigned to ν(C=O) of the pyrazolone ring and C=N, respectively. Bands in the region 310–325 are associated with M–Cl stretching vibrations and 450–520 cm^{-1} to M–O stretching vibrations [69].

IR spectral data of the ligands reported by Raman *et al.* [73] (*i.e.* neutral tetradentate ligand derived from acetoacetanilido-4-aminoantipyrine and 2-aminophenol/2-aminothiophenol) show bands around 3180 cm^{-1} for ν(O–H- - - N=), 1680 cm^{-1} for

ν(C=O) and at 1520 cm^{-1} for ν(C=N), which decrease 30–80 cm^{-1} in the spectra of the complexes due to coordination.

Agarwal [9] reported IR bands due to O=V=O group appearing at 960 cm^{-1} for ν_{asy}(V=O), 800 cm^{-1} for ν_{sym}(V=O) and 250 cm^{-1} for ν(O=V=O), indicating that the VO_2 is virtually linear with the possibility of H-bonding between –OH and O=V=O. The IR spectrum of free ligand shows ν(C–O) at 1330 cm^{-1}, raised by 8–37 cm^{-1} in the spectra of the complexes. A band at 1028 cm^{-1} is due to ν(N–O) of oximino group.

The IR spectrum of ligand (4-aminoantipyrine and oxime) shows bands at 1689 cm^{-1} and 1600 cm^{-1} due to ν(C=N) oxime and ν(C=N) pyrazone, downshifted by 9–49 cm^{-1} due to coordination [69]. The IR spectra of vanadyl complexes show a band at 960 cm^{-1} due to ν(V=O), suggesting monomeric (V=O). The presence of coordinated water is suggested by the very broad absorption centered at 3450 cm^{-1} in the IR spectrum. Bands at 930 and 770 cm^{-1} may be attributed to rocking and wagging of coordinated water. In acetate complexes, two bands were observed at 1630 and 1390 cm^{-1} assigned to ν_{asym} and ν_{sym} (COO^-).

5.3. *ESR spectroscopy*

The ESR spectra of metal chelates provide information about hyperfine and superhyperfine structures which are important in studying the metal ion environment in the complexes, *i.e.* the geometry, nature of the ligating sites from the Schiff base. The X-band ESR spectra of [CuLCl] [72] (L = salicylidene-4-aminoantipyrine-aniline) in DMSO at 300 K show one intense absorption at high field, which is isotropic due to tumbling of the molecule. However, at 77 K well-resolved peaks with low intensities in the low field region and one intense peak in the high field region are observed. The *g*-tensor values of the copper complexes coincide with related systems, suggesting that the complexes have square-planar geometry and the system is axially symmetric. Also, the exchange interaction coupling constant (G) and the covalent bonding parameters α^2, β^2 and γ^2 have been calculated.

ESR spectra of $CuLCl_2$ [75] (L = tetraaza macrocyclic Schiff base synthesized from 1, 2-(diimino-4-antipyrinyl)-1,2-diphenylethane and *o*-phenylenediamine) suggest square-planar complex with the unpaired electron predominantly in the $d_{x^2-y^2}$ orbital. The observed $A_\parallel$ and higher $g_\parallel$ values indicate that there is slight distortion from planarity. The bonding parameter of the complex is also calculated by simplified molecular orbital theory [86]. The ESR spectrum of vanadyl complex at room temperature contains a typical eight line pattern showing a single vanadium, *i.e.* monomer. In the frozen state, it shows two types of resonances, one due to the parallel features and the other to the perpendicular features which show an axially symmetric anisotropy with well resolved 16-line hyperfine splitting characteristic of an interaction between the electron and the vanadium nuclear spin. The observed order of the parameters $A_\parallel > A_\perp$ and $g_\parallel = 1.98 < g_\perp = 2.04$ indicates that the complex is square pyramidal [87–89]. The observed $g_\parallel$ 2.2569 of Cu(II) complex [84] is less than 2.3 suggesting significant covalent character of the metal ligand bond. The trend $g_\parallel = (2.2569) > g_\perp = (2.0225) > g_e = (2.0023)$ observed suggests that the unpaired e^- is localized in the $d_{x^2-y^2}$ orbital. The bonding parameters were also calculated. The observed $K_\parallel$ $(0.8475) > K_\perp (0.4775)$ indicates the absence of significant in-plane bonding. The *g*-tensor values of the CuL complex

(L = acetoacetanilido-4-aminoantipyrine-2-aminophenol) derived from the observed value and ESR parameters indicate square-planar geometry [73]. The observed G value (4.4) suggests that the local tetragonal axes are aligned parallel or slightly misaligned. The ESR spectrum of vanadyl at room temperature contains a typical eight line pattern for a single vanadium. The various parameters calculated indicate that the unpaired electron is present in the d_{xy} orbital with square-pyramidal geometry around vanadium.

5.4. *^{1}H-NMR spectroscopy*

In addition to UV-Vis and IR studies, some diamagnetic complexes and their ligands have been characterized by NMR spectroscopy. The proton NMR spectrum of ligand derived from 1,2-(diimino-4-antipyrinyl)-1,2-diphenylethane, *o*-phenylenediamine and salicylaldehyde showed the following signals: C_6H_5 as a multiplet at 6.9–7.5 δ, $=C-CH_3$ at 2.3–2.5 δ, $-N-CH_3$ at 3.1–3.2 δ and azomethine proton at 9.8–9.9 δ. The peak at 13.4 δ is attributed to the intramolecular bonded phenolic OH group present in salicylaldehyde [75]. The proton NMR spectra of the zinc Schiff-base complex show the following signals: phenyl multiplets at 6.9–8.6 δ, $=C-CH_3$ at 2.2 δ, azomethine at 6.2 δ. The peaks at 13.4 δ and 9.8 δ are attributed to the enolic and phenol OH^- group. The absence of these two peaks in the zinc complex indicates loss of OH proton due to complexation [73].

The azomethine proton in the Zn complex is shifted downfield compared to free ligand, suggesting deshielding of the azomethine group due to coordination with zinc. There is no appreciable change in the other signals of this complex.

6. Redox and thermal behavior

6.1. *Redox properties*

In order to characterize the redox processes on the ligand and complexes, electrochemical investigations in suitable solvents are performed.

The cyclic voltammogram of the copper complex of the ligand derived from acetoacetanilido-4-aminoantipyrine and 2-aminophenol/2-aminothiophenol [73] in 1.0 to 1.2 V potential range showed a well-defined redox process corresponding to the formation of the Cu(II)/Cu(I) couple at $Ep_a = 0.21$ V and the associated cathodic peak at $Ep_c = 0.16$ V. This couple is reversible with $\Delta E_P \sim ca.$ 0.05–0.06 V and $Ip_c/Ip_c \approx 1$ corresponding to a simple one-electron process. The complex also shows a quasi reversible signal in the negative region characteristic of Cu(II)/Cu(I) at $Ep_c = -0.68$ V with associated anodic peak at $Ep_a = -0.48$ V for Cu(I)/Cu(II) oxidation. The cyclic voltammogram for vanadyl complexes show two well-defined one e^- redox peaks corresponding to formation of V(IV)/V(V) and V(IV)/V(III) [91, 92]. The voltammetric data of all the copper complexes for the Cu(II)/Cu(III) couple are given; from the data, for Ep_a values (0.54–0.62 V) and associated Ep_c values (0.48–0.56 V), this couple is reversible with $\Delta E_P \sim 0.05$–0.06 V and the ratio of cathodic to anodic peak currents Ip_c/Ip_a corresponds to a simple one-electron process.

The transfer coefficients (α_n) for irreversible processes calculated from plots of peak potential *versus* logarithmic values of the scan rate were fractioned. The standard rate constant for all reversible processes employing the equation

$$i_p = nFACks \exp[-\alpha_n/RT(E - E_i)]$$

are low, confirming slow e^- transfer, and in turn irreversible e^- transfer.

Chronocoulometric experiments were carried out and diffusion coefficient (D) of the complexes was calculated from the slope of the straight line obtained for Q_d *versus* $t^{1/2}$ plot. The I_p values were calculated by substituting the diffusion coefficient (D) from CV results in the Randles Sevcik equation for irreversible processes

$$i_p = 2.9 \times 10^5 \times n(\alpha_n)^{1/2} AD^{1/2} Cv^{1/2}$$

where n = number of electron transfer, A = electrode area, C = concentration of the electrolyte, D = diffusion coefficient, v = scan rate and α_n = transfer coefficient.

The experimental and calculated i_p values are equal, confirming that $Cu(0) \rightarrow Cu(II) + 2e^-$ is an irreversible CT process. The CV of the copper complex synthesized by Raman *et al.* [75] shows a reversible peak for Cu(II)/Cu(III) at $Ep_a = 0.38$ V with direct cathodic peak for Cu(III)/Cu(II) at $Ep_c = 0.32$ V. The nickel complex shows a redox process corresponding to formation of Ni(II)/Ni(III) couple at $Ep_a = 0.98$ V and associated cathodic peak at $Ep_c = 0.93$ V. This couple is reversible with $\Delta Ep = 0.05$ V and $Ip_c/Ip_a = 0.66$ corresponding to a one-electron process. Similarly, cobalt complex shows a peak for formation of the Co(III)/Co(II) couple as a reversible, one-electron transfer. The CV of oxovanadium complex shows two well-defined, one-electron redox peaks corresponding to formation of V(IV)/V(V) and V(IV)/V(III) couples [55, 67].

6.2. *Thermal properties*

Very few references are available on thermal properties of 4-aminoantipyrine derived metal complexes. Polymorphism is very common with different m.p., solubility, chemical reactivity and stability. The thermal behaviors of $(Ln(L)_2ClO_4)$ (Ln = La, Pr, Nd or Sm) and $(Ln(HL)_4)(ClO_4)_3$ (Ln = Gd, Tb, Dy, Ho or Y) show that La, Pr, Nd and Sm complexes are more stable (up to 300°C) than Gd, Tb, Dy, Ho and Y complexes (up to 240°C). The La and Pr complexes undergo decomposition in two stages as denoted by DTG peaks around 350 and 460°C. The DTG peaks shown by Nd and Sm are 350, 400 and 480°C. The complexes of Gd, Tb, Dy, Ho and Y undergo decomposition in three stages as represented by the DTG peaks around 295–320, 415–445 and 490–505°C; decomposition of all complexes is complete at 520–580°C and the respective stable rare-earth oxides are formed [24, 52].

The thermal studies of Th(IV) complexes [28] of CAAPS do not show the presence of water molecules, either in or out of the coordination sphere. The pyrolysis curves of these complexes suggest that in the first step, DPSO evaporated in the 155–170°C temperature range. The break in the TG-curves at ~310°C indicates that the primary ligand (CAAPS) has been lost. In the case of nitrate complex at 510°C, ThO_2 is the end product. From the pyrolysis curve of $Th(ClO_4)_4$2(CAAPS)·DPSO at 170°C, DPSO molecule has been lost. At 220–250°C, one CAAPS has been lost.

Finally, at 550°C, ThO_2 is the end product [90]. Thus, in the case of $[ThX_4 \cdot (L) \cdot DPSO]$, the decomposition scheme is:

$$ThX_4 \cdot (CAAPS) \cdot DPSO \rightarrow ThX_4 \cdot (CAAPS) \rightarrow ThX_4 \rightarrow ThOX_2 (X = Cl, Br \text{ or } NCS)$$
$$Th(NO_3)_4 (CAAPS) DPSO \rightarrow Th(NO_3)_4 (CAAPS) \rightarrow Th(NO_3)_4 \rightarrow ThO_2$$
$$Th(ClO_4)_4 \cdot 2(CAAPS) \cdot DPSO \rightarrow Th(ClO_4)_4 \cdot 2(CAAPS) \rightarrow Th(ClO_4)_4 (CAAPS) \rightarrow ThO_2$$

7. Antimicrobial aspects of 4-aminoantipyrine based ligands and their complexes

One reason why the literature concerning 4-aminoantipyrine derived complexes is richer and more diverse than other pyrazole rings is the higher biological activity. 4-Aminoantipyrine derived complexes show antimicrobial, anti-malarial and anti-tumorous activities.

The antimicrobial activity of Schiff base 4-aminoantipyrine derivatives were tested against *Staphylococcus aureus*, *Klebsilla pneumoniae*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Bacillus subtilis*. The complexes showed higher inhibitory activity than the ligands and have higher activity than ampicillin, except for *Klebsilla pneumoniae* and *Pseudomonas aeruginosa* [21].

Rosu *et al*. reported biological activity of ligands and their copper complexes [52] on samples of *E. coli*, *K. pneumoniae*, *A. boumanii*, *S. aureus*, *P. aeruginosa* and *Candida sp*. The Schiff-base ligand and its copper complex exhibited high bactericidal activity towards *E. coli* and *A. boumanii*, good activity against *S. aureus* and *E. coli*, proving their potential usefulness as broad spectrum antimicrobial agents. The biocidal activity studies of the oxovanadyl complexes and the free ligands towards three gram-positive bacteria: *B. subtilis*, *Sarcina lutea* and *S. aphylococcus*; seven gram negative bacteria *viz E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. typhi*, *Serratia marcescens*, *Shigella sonnie* and *Proteus mirabilis*; three fungal species: *Aspergillus flarus*, *Penicillium chrysogenum* and *candida albicans*, have been studied by Ismail *et al*. [7]; the activity is related to the nature and structure of the complexes. The copper complex was the most promising broad spectrum antimicrobial agent due to the presence of coordinated anion and bridged $O–H^-$ with higher antimicrobial activity than the other complexes, superior to all other complexes against all the test organisms except *P. aeruginosa*.

Some of the isolated metal-4-aminoantipyrine derivatives were tested for activity against a variety of microorganisms, and some other biotests have also been performed. In most tests, the activity of the complexes is comparable to free 4-aminoantipyrine derivatives. In certain examples, the activity increased but there is no evidence of further clinical tests.

The efficacy of metal-based therapeutic agents changes considerably by making small changes in the Schiff-base ligand attached to the metal [93].

The *in vitro* antimicrobial activity of ML [73] (L = acetoacetanilido-4-aminoantipyrine and 2-aminophenol/2-aminothiophenol, where M = Cu(II), Ni(II), Co(II), Zn(II) and VO(II)) and $MnL \cdot 2H_2O$ were tested against bacteria such as *S. typhi*, *S. aureus*, *K. pneumoniae*, *B. subtilis*, *S. flexneri* and *P. aeruginosa* and the fungi *A. niger* and *R. bataicola*. From the data the inhibition zone of the metal chelates is higher than that of the ligand. Such increased activity of the metal chelates is due to the lipophilic nature of the metal ion in complexes. Furthermore, the mode of action

of the compounds may involve the formation of a hydrogen bond through the azomethine nitrogen atom with the active canters of all the constituents, resulting in interference with normal cell process.

The minimum inhibitory concentration (MIC) value of copper(II) complexes derived from salicylidene-4-aminoantipyrine and aniline derivatives were determined for five bacteria *viz*. *S. aureus*, *K. pneumoniae*, *S. typhi*, *P. aeruginosa* and *B. subtilis* by serial dilution. A comparative study of the ligands and their copper complexes indicates that the copper complexes exhibit slightly higher antibacterial activity than free ligands and ampicillin [21]. Such increased activity of the complexes can be explained on the basis of Overtone's concept and Tweedy's concept.

Raman *et al.* [75] synthesized a tetraaza macrocyclic Schiff base and its metal complexes derived from 1,2-(diimino-4-antipyrinyl)-1,2-diphenylethane and *o*-phenylenediamine in ethanol. For *in vitro* antibacterial screening the investigated compounds, ligand and uncomplexed metal salts ($CuCl_2 \cdot 2H_2O$, $NiCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $ZnCl_2$, $VOSO_4 \cdot H_2O$) were screened against six bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Shigella flexneri*. The observed MIC values indicate that most of the uncomplexed metal salts exhibit higher antibacterial activity than the synthesized compounds. According to the chelate hypothesis the compound-organism interaction visualized in the equilibria below.

$$\underset{\text{(Ligand)}}{\text{L}} + \underset{\text{(Organism)}}{\text{R}} \leftrightarrows \underset{\text{(Ligand-Organism complex)}}{\text{LR}}$$

$$\underset{\text{(Metal chelate)}}{\text{ML}} + \underset{\text{(Organism)}}{\text{R}} \leftrightarrows \underset{\text{(Metal bridged-ligand-Organism complex)}}{\text{RML}}$$

$$\underset{\text{(Metal chelate)}}{\text{MX}_2} + \underset{\text{(Organism)}}{\text{R}} \leftrightarrows \underset{\text{(Metal-Organism complex)}}{\text{RMX}_2}$$

The above mentioned equilibria suggest that the antimicrobial activity of the compound depends on the ability to form a compound-organism complex in the following order:

$$\text{uncomplexed metal salt} > \text{metal chelate} > \text{free ligand}$$

clearly indicating that the uncomplexed metal salts have greater ability to form the compound-organism complex. Higher activity of the metal chelates is due to the increased lipophilicity from inclusion of metal ion with the Schiff base.

Most of the newly synthesized compounds were tested for antibacterial activity *in vitro* against bacterial strains such as *S. aureus*, *E. coli*, *K. pneumoniae* and fungi *C. albicans* and *R. stolonifer* employing the nutrient agar disc diffusion method in DMSO. The results showed that all compounds exhibited marked activity against bacteria in comparison to amphotericin, which was taken as a standard drug. From the data, nickel complex exhibits higher activity against *E. coli* and *R. stolonifer*, copper complex against *S. aureus* and *K. pneumoniae* and cobalt complex against *C. albicans*. The results showed the degree of inhibition varied with the tested compounds [23].

8. DNA cleavage studies of 4-aminoantipyrine derived Schiff-base metal complexes

Investigations of interaction of DNA with small molecules are basic in the design of new types of pharmaceutical molecules. Some metal complexes interact with DNA and

induce breakage of DNA strands. Thus, to cancer genes, after DNA strand cleaves, the DNA double strands break. The replication ability of the cancer gene is destroyed. Many complexes including the platinum group have been synthesized and tested in a number of biological systems after the discovery of cis-platin. A number of metal complexes of 4-aminoantipyrine derived ligands have been studied in view of their possibility to lead to advanced functional materials, tuning the redox potentials, affinity towards DNA, and specificity for the DNA base sequence recognition [23, 55, 66].

DNA cleavage was conducted using CT DNA by gel electrophoresis with the corresponding metal complexes in the presence of H_2O_2 as oxidant. We have done a lot of work in the CT DNA cleavage studies of 4-aminoantipyrine derived Schiff bases and their complexes [66]. Cu(II), Ni(II) and Co(II) complexes cleave DNA as compared to control DNA, while Mn(II), Zn(II), VO(IV), Hg(II) and Cd(II) complexes do not cleave DNA in the presence of H_2O_2.

Agarose gel to conduct electrophoresis with such systems including DNA alone, DNA-H_2O_2-Cu(II) complex, DNA-H_2O_2-Co(II) complex, DNA-H_2O_2-Ni(II) complex and DNA-H_2O_2-Zn(II) complex was prepared under the same condition and kept 2 h in order to eliminate the influence of the reaction speed. This result reveals that cleavage of DNA in Cu(II) system is more efficient than other systems. All other systems showed the same electrophoretic behavior and less cleavage activity against CT DNA [94].

Agarose gel to conduct electrophoresis for three oxovanadium(IV) Schiff-base complexes [55] $[VO(Phen)(L)]SO_4$ where L = [(benzylidene)amino]antipyrine (**1a**), 4[(cinnamalidene)amino]antipyrine (**1b**) and 4[(2-chlorobenzylidene)amino]antipyrine (**1c**) including DNA alone, DNA-H_2O_2-**1a** complex, DNA-H_2O_2-**1b** complex and DNA-H_2O_2-**1c** complex which were prepared under the same condition. Damage of DNA in **1a** could be attributed to the cleavage of DNA. The **1b** and **1c** systems showed the same electrophoretic behavior and less cleavage activity against CT DNA.

The available literature reveals that the cleavage efficiency of the complexes compared to controls is due to their efficient DNA–binding ability. The metal complexes are able to convert super coiled DNA into open circular DNA. General oxidative mechanisms proposed for DNA cleavage by hydroxyl radicals *via* abstraction of a hydrogen from sugar units predict the release of specific residues arising from transformed sugars, depending on the position from which the hydrogen is removed [94, 95]. The cleavage is inhibited by the free radical scavengers implying that hydroxyl radical or peroxy derivatives mediate the cleavage [96]. The reaction is modulated by a metallocomplex bound hydroxyl radical or a peroxo species generated from the co-reactant H_2O_2.

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