



## 4-Aminoantipyrene: A Significant Tool for the Synthesis of Biologically Active Schiff Bases and Metal Complexes

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### ABSTRACT

Schiff bases derived from 4-aminoantipyrene play a vital role in biological and pharmacological activities. Knowing the importance of 4-aminoantipyrene Schiff bases and their analogues wide varieties of bioactivities like analgesic, antipyretic, anti-rheumatic, antimicrobial and anti-inflammatory have been widely studied. Properties of 4-aminoantipyrene to coordinate with metals is varied by condensing it with aldehydes, ketones, thiosemicarbazides and carbazides etc. Schiff base ligand and metal complexes of 4-aminoantipyrene has been studied exhaustively. This review summarizes the synthetic utility, biological activities and pharmacological significance of Schiff bases and metal complexes derived from 4-aminoantipyrene.

**Keywords:** 4-aminoantipyrene, Schiff bases, ligands, metal complexes, biological activity.

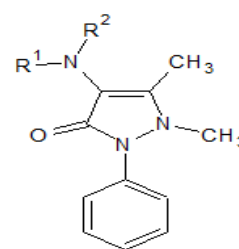
### INTRODUCTION

Now a day's chemists are very much focused on the Schiff bases derived from heterocyclic ring with carbonyl compounds as its important special centre of attraction in many areas like biological, medicinal, analytical and pharmacological field.<sup>1-3</sup> Among them 4-aminoantipyrene based heterocyclics had a great importance as it is abundant in nature and have wide pharmacological activities,<sup>4</sup> 4-Aminoantipyrene is a temperature reducing pyrazole derivative.<sup>5</sup> It is used in the preparation of azo dyes.<sup>6</sup> 4-Aminoantipyrene also has been used for the protection against oxidative stress as well as prophylactic of some diseases including cancer, and these are important directions in medical applications.<sup>7</sup> Several derivatives of antipyrene were also evaluated as analgesic,<sup>8</sup> anti-inflammatory,<sup>9</sup> antimicrobial,<sup>10</sup> and anticancer activity,<sup>11-13</sup> These are also strong inhibitors of cyclooxygenase isoenzymes, platelet thromboxane synthesis, and prostaglandin synthesis,<sup>14</sup> which catalyze the rate-limiting step of prostaglandin synthesis. Aminoantipyrene derivatives are commonly managed intravenously to detect liver disease<sup>15</sup> in clinical treatment. Thorough literature survey reveals that more attention has been given to Schiff's base and metal complexes derived from 4-aminoantipyrene with several aldehydes.

4-aminoantipyrene has an N-phenyl group and a -CH<sub>2</sub> group on either side of a polar carbonyl group, thus resembles to N-substituted amides. The carbonyl group in 4-aminoantipyrene is a potential donor due to the large dipole moment (5.48 D) and strong basic characters.<sup>16</sup> Since 4-aminoantipyrene has an additional potential coordination site in the amino nitrogen, it was considered worthwhile to study the complexes of this ligand.

Generally, the electron withdrawing and electron releasing nature and the position of substituents present

in the phenyl ring affect the antimicrobial activities; the presence of substituents at the *o*-position lowers the antimicrobial activity whereas the substituents at the *m*- and *p*-positions give higher antimicrobial activity. Inhibition is enhanced with the introduction of an electron withdrawing nitro group in the phenyl ring.<sup>17</sup> Recently 4-aminoantipyrene and 4-methylantipyrene has been found to correlate with the analgesic effect of dipyrone.<sup>18</sup> Dipyrone and some 4-aminoantipyrene derivatives have a high potential to attenuate or prevent the anti-platelet effects of aspirin.<sup>19</sup> Xiong<sup>20</sup> obtained and analyse the electronic structures of aminoantipyrene and its derivatives (**1**).



(1)

Where:  $R^1 = -H, -CH_3, -CH_2SO_3, -CHO, -COOCH_3$ ,  $R^2 = -H, -CH_3$

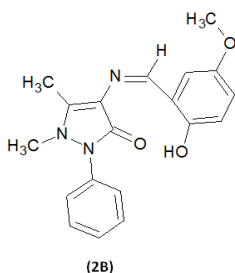
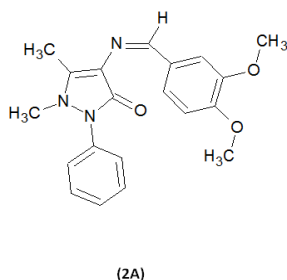
Schiff bases and metal complexes of 4-aminoantipyrene are also known for their great variety of applications in the area of catalysis<sup>21,22</sup> and biological activity ranging from antitumour, fungicide, bactericide, anti-inflammatory and antiviral activities.<sup>23-26</sup> Reports on drugs showed increased activity when administered as metal complexes rather than as organic compounds.<sup>27,28</sup> Investigation on the interaction of DNA with small molecules is also important in the design of new types of pharmaceutical molecules. Some kinds of metal complexes interact with DNA that could induce breakage of DNA strands.<sup>29,30</sup>

The coordination properties of 4-aminoantipyrine have been modified to give new ligands formed by the reaction with aldehydes, ketones, thiocarbazides and carbazides etc.<sup>31,32</sup> The coordinating property of Schiff bases of 4-aminoantipyrine have attracted considerably. Chemists from co-ordination and medicinal fields have extensively studied 4-aminoantipyrine. Many metal complexes has powerful antimicrobial activities and are already in common day-to-day use in medicinal field such as silver bandages for treatment of burns, zinc antiseptic creams, bismuth drugs for the treatment of ulcers and metal clusters as anti-HIV drugs. The most spectacular advances in medicinal chemistry have been made when heterocyclic compounds played an important role in regulating biological activities. A wide range of metal complexes are already in clinical use and encourage further studies for new metallodrugs such as anticancer, anti-viral antiparasitic. The transition metal complexes of 4-aminoantipyrine and derivatives have been extensively examined due to their wide applications in various fields like biological, analytical and therapeutical.<sup>33,34</sup> 4-aminoantipyrine has played an important role in organic and inorganic chemistry; it forms many Schiff bases and stable complexes with many transition metal ions.

### Schiff bases Derived from 4-Aminoantipyrine

Schiff bases are considered as "Privileged ligands", because they are easily prepared by the condensation between aldehydes and amines. These have been synthesized from a variety of compounds, such as aminothiazoles, 2-hydroxy-1-naphthalaniline, aminosugars, aromatic aldehydes, isatin, triazole ring, thiosemicarbazides, amino acids, and pyrazolone.<sup>35-37</sup> Studies of a new kind of chemotherapeutic compounds are now attracting the attention of biochemists.<sup>38,39</sup>

Aly<sup>40</sup> synthesized a new series of 4-substituted-pyrazole, pyrrolo [3,2-c]pyrazole, acetamide, pyrrole, ethoxythiourea and pyrazolo[4,3-d]imidazole and screened for excellent promising biological activities. Mostafa<sup>41</sup> synthesized a new series of heterocycles incorporating antipyrine moiety starting from 4-aminoantipyrine, and their anticancer activity against human tumor breast cell line (MCF7) evaluated. Two new Schiff base ligands 4-[(1E)-(3,4-dimethoxyphenyl)methylene]amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (**2A**) and 4-[(1E)-(2-hydroxy-5-methoxyphenyl)methylene]amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (**2B**) have been prepared by Hayvali<sup>42</sup>.



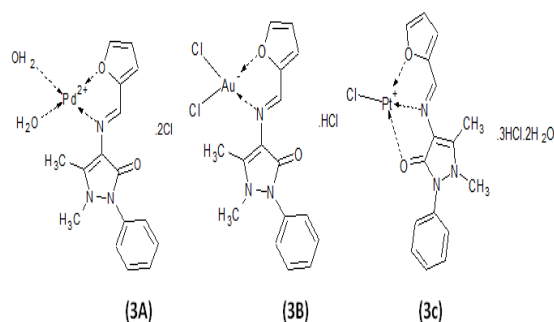
Schiff bases derived from 4-aminoantipyrine and vanillin were synthesized by Chanda<sup>43</sup> with their antibacterial activity evaluation. The Schiff-base derived from picolinaldehyde N-oxide and 4-aminoantipyrine, and its copper (II) complex: has been prepared by Liang<sup>44</sup>. Catalina<sup>45</sup> prepared some Schiff bases of isatin or substituted isatins by reaction with 4-aminoantipyrine and tested *in-vitro* for antimicrobial antioxidant activity. All the results were found in agreement with the 'Lipinski's rule of five' having desirable molecular properties for drug likeness.

Based on the above information and due to our interest in 4-aminoantipyrine as a biologically active pharmacophore Raman<sup>46</sup> synthesized Schiff base derived from 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and *o*-phenylenediamine. Spano<sup>47</sup> prepared 2,3-dimethyl-1-phenyl-4-(1-admantanecarboxamido)-5-pyrazolone and tested for analgesic and antipyretic activity. Mohanram<sup>48</sup> condensed 4-aminoantipyrine by Betti reaction to formulate novel biologically potent moieties. They synthesized 4-aminoantipyrine derivatives and assayed for anti-inflammatory, anthelmintic and also compared these results with 'Lipinski's rule of five'. Prakash<sup>49</sup> have synthesized Schiff base ligands using vanillin, 4-aminoantipyrine, anthranilic acid, *o*-phenylenediamine and furfural, to prepare transition metal complexes of Zinc (II). In light of research, it have been concluded that the precise nature of the Schiff base ligands is of remarkable importance in the interaction of the complex with the DNA molecule.

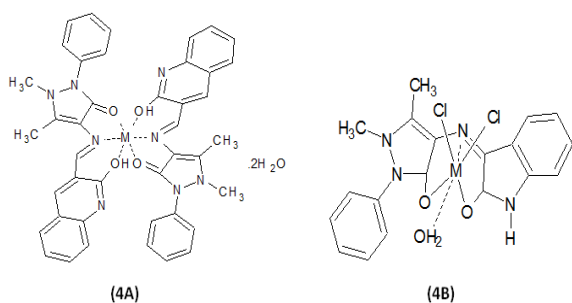
### Metal Complexes Derived from 4-Aminoantipyrine

Metal complexes of 4-Aminoantipyrine have been known to possess potential diverse applications in biological, clinical, analytical, and pharmacological areas.<sup>50</sup> Studies on a new kind of chemotherapeutics is attracting the attention of biochemists<sup>51,52</sup> since last decade. The coordinating property of Schiff bases of 4-aminoantipyrine have attracted significantly because of their pharmaceutical and therapeutic importance. In light of the interesting variety of biological activities seen in compounds containing antipyrine group and azomethine linkages, it was thought by chemists to synthesise new compounds having all of above functionalities present simultaneously in one structure. MIC values of the Schiff bases and its metal complexes indicate that metal complexes exhibit higher antibacterial activity than the free ligand. Such increased activity of the metal chelates was explained on the basis of Overtone's concept and chelation theory. Raman<sup>53</sup> reported the synthesis of transition metal complexes of Cu (II) Ni(II), Co(II), Mn(II), Zn(II) And VO(II) using Schiff bases of 4-aminoantipyrine derived from 1-phenyl-2,3-dimethyl-4(4-aminopantane-2-one)-pyrazole-5-one with 2-aminophenol/2-aminothiophenol and evaluation of biological potential. Pt(IV), Au(III) and Pd(II) complexes(**3A**), (**3B**), (**3C**) of Schiff bases derived from 2-furaldehyde and 4-amino antipyrine have been reported by Al-Sair<sup>54</sup> their antibacterial activity

data showed the metal complexes more potent than the parent Schiff base ligand.



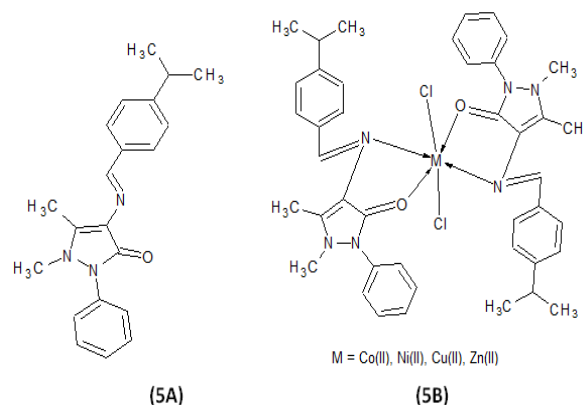
In view of the investigations on Schiff base-metal complexes Rosa and colleagues<sup>55</sup> presented the synthesis of Cu(II) complexes derived from Schiff base ligand obtained by condensation of 4-aminoantipyrene with 2-hydroxybenzaldehyde and terephthalic aldehyde, they continued in their studies<sup>56</sup> by use other salt of Cu(II) as well as other complexes of V(IV) and Ni(II), and synthesized<sup>57</sup> new complexes of Cu(II) with Schiff bases obtained by the condensation of 4-aminoantipyrene with 2-hydroxy-4-methoxy-benzaldehyde. Kurdekar<sup>58</sup> have reported the synthesis and anticonvulsant evaluation of metal complexes (4A) and (4B) of Co(II), Ni(II), Cu(II), Zn(II) and ligands derived from 4-aminoantipyrene-based Schiff-bases.



Efforts were taken by Prakash<sup>59</sup> for the synthesis of transition metal complexes of metal (II) ions by Schiff base ligands derived from vanillin, 4-aminoantipyrene and *o*-phenylenediamine. *In-vitro* activity screening also performed against bacterial strains.

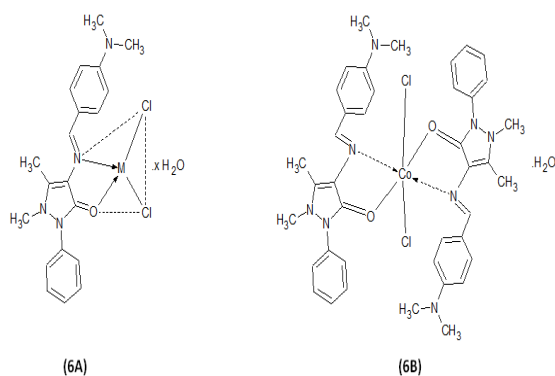
The *in-vitro* biological activities and DNA cleavage activity of the ligand and its complexes of metal (II) ions showed that all the complexes have completely cleaved the DNA which were prepared from Schiff base ligand obtained via condensation of imidazole 2-carboxaldehyde 4-aminoantipyrene, and 2-aminophenol by Pearl.<sup>60</sup> The potentially novel copper (II) complexes have been synthesized, screened *in-vitro* by Gopalakrishan<sup>61</sup> from the macrocyclic Schiff bases derived from  $\beta$ -ketoanilides, 4-aminoantipyrene and *o*-phenylene diamine. The complex  $[\text{Cd}^{\text{II}}\text{L}_2(\text{NO}_2)_2]$  (L= 4-aminoantipyrene) was synthesized by Rajsekar.<sup>62</sup> Antony<sup>63</sup> prepared a Schiff bases derived from 4-aminoantipyrene and dihydropyrimidone and their complexes with Cu (II), Co (II) and Cr (III) ions obtained from vanillin, and reported antimicrobial activity test against pathogens. David<sup>64</sup>

reported the synthesis and antimicrobial activity of Schiff bases prepared from 4-aminoantipyrene and cuminaldehyde or 4-isopropylbenzaldehyde (5A) and their complexes (5B) of 3d transition metal (II) ions.



Metal complexes from Schiff base ligand were prepared via condensation of 4-aminoantipyrene and benzyl by Lateef.<sup>65</sup> Antibacterial activity results showed that only Cd (II) complex have a high activity for *E. coli*. Boghaei<sup>66</sup> synthesized Ni (II) and Cu (II) Schiff base complexes with  $\text{N}_2\text{O}_2$  and  $\text{N}_2\text{O}$  donor sites. El-Ajaily<sup>67</sup> studied the antibacterial activities of the Schiff base derived from the salicylaldehyde and histidine and Mn (II), Co (II), Ni (II), Cu (II) and Cd (II) complexes and tested on some pathogenic bacteria. Schiff base complexes of Ni(II), Cu(II), Rh(III), and Pt (IV) with 4-dimethylaminobenzaldehyde and 4-aminoantipyrene were prepared by Maihub.<sup>68</sup> Bioactivities of the ligand 4-((2-mercapto-1H-benzimidazol-1yl) methylamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one derived from 2-Mercapto benzimidazole, formaldehyde and 4-aminoantipyrene as well as metal (II) complexes have been carried out by Bhava<sup>69</sup> against various pathogens. Kumari<sup>70</sup> reported synthesis and biological screening of Schiff base ligand derived from 4-aminoantipyrene and 5-bromo salicylaldehyde and transition metal complexes of Cu (II), Ni (II), Co(II), Zn(II) and VO (IV) exhibited significant activity against microorganisms. A Schiff base ligand containing two bioactive moieties, 4-aminoantipyrene and pyrrole namely, 4-(2-pyrrolyl- methylideneamino)antipyrene and its copper (II) complexes were synthesized by Ismail<sup>71</sup> and *in-vitro* biological activity screening of the compounds against bacterial and fungal species have been studied. Cobalt (II) complexes were prepared by Radhakrishnan<sup>72</sup> from Schiff bases 1,2-(diimino-4'-antipyrynyl)ethane and 4-N-(4'-antipyrylmethylidene) aminoantipyrene.

Zeng Zh-Zh<sup>73</sup> synthesised a new ligand of 1-(4-Aminoantipyrene)-3-tosylurea and its lanthanide (III), Nd(III), Sm(III) and Eu(III)] complexes with *in-vitro* activity evaluations. These complexes were found to possess potent antioxidant activity. A ligand 4-[(4-Dimethylamino-benzylidene)-amino]-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-on have been synthesized by the reaction of 4-aminoantipyrene with 4-dimethylamino. The complexes (6A), (6B) of Co(II), Zn(II) Cd(II) and Hg(II) with this ligand have been prepared by Bedeui.<sup>74</sup>



The complexes of 3d series, synthesized by rajasekar<sup>75</sup> with the ligands 4-aminoantipyrine and thiocyanate ion and biological activities of 4-aminoantipyrine and its complexes were tested against some micro-organisms. The Cadmium (II) complexes of the Schiff base 1,2-di(imino-4'-antipyrinyl)ethane have been synthesized by Radhakrishnan.<sup>76</sup> Maurya<sup>77</sup> reported the synthesis of hexacoordinated mixed-ligand dinitrosyl complexes of molybdenum(0) of the composition  $[Mo(NO)_2(L)(OH)]$ , where LH = N-(3'-methyl-1'-phenyl-4'-valerylidene-2'-pyrazolin-5'-one)-4-aminoantipyrine, N-(4'-benzoylidene-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one)-4-aminoantipyrine, N-(3'-methyl-1'-phenyl-4'-propionylidene-2'-pyrazolin-5'-one)-4-aminoantipyrine, N-(4'-acetylidene-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one)-4-aminoantipyrine or N-(4'-iso-butyrylidene-3'-methyl-1'-phenyl-2'-pyrazolin-5'-one)-4-aminoantipyrine directly from molybdate(VI).

It is well known that the existence of metal or metal ions bonded to biologically active compounds may enhance their activities. The complexes of different Schiff bases (5-methyl 2-hydroxy acetophenone morpholine-N-thiohydrozone, 5-chloro2hydroxy acetophenone-morpholine-N-thiohydrazone and 5-methyl 2-hydroxy acetophenone antipyrine) with Mn (III) and Mn (II) have been synthesized by Nizami.<sup>78</sup>

Investigation on the interaction of DNA with small molecules is important in the design of new types of pharmaceutical molecules. Co(II), Ni(II), Cu(II) and Zn(II) complexes with Schiff base derived from furfurylidene-4-aminoantipyrine and 2 aminobenzothiazole have been synthesized and characterized by Antony.<sup>79</sup>

In contrast to the considerable growth of literature on the biologically active Schiff base derivatives of 4-aminoantipyrine, neutral complexes of Co(II), Ni(II), Cu(II), and Zn(II) have been synthesized by Nair<sup>80</sup> from the Schiff bases derived from 3-nitrobenzylidene-4-aminoantipyrine and aniline, *p*-nitro aniline and *p*-methoxy aniline. The transition metal complexes of Cr(III), Co(II), Ni(II) and Zn(II) were synthesized by Rajasekar<sup>81</sup> with the ligands 4-aminoantipyrine and azide ion. Tridentate chelate complexes of Co(II), Ni(II), and Cu(II) have been synthesized by Tharmaraj<sup>82</sup> from 4-[N,Nbis-(3,5-dimethylpyrazolyl-1-methyl)]aminoantipyrine. The antimicrobial activities of the ligands and metal complexes tested

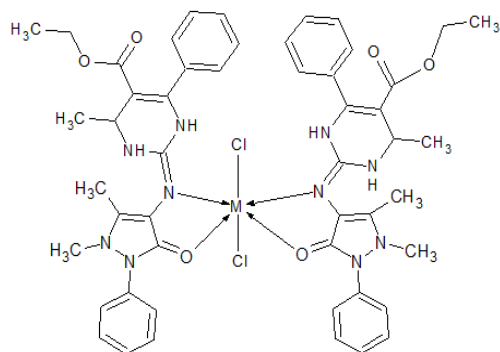
against the bacteria and the fungus. Compounds  $[Cu(L1)2]$  and  $[Cu(L2)2]$  with Schiff base ligands of 4-aminoantipyrine and substituted salicylaldehydes, were synthesized by Subramanian.<sup>83</sup>

Schiff bases itself have some antimicrobial activity which have been enhanced by chelating it with metal ion.<sup>84</sup> Kulandaisamy<sup>85</sup> reported the synthesis and antimicrobial studies of transition metal complexes of Cu(II), Ni(II), Co(II), Zn(II) and VO(II). The Schiff base and its metal complexes gave good *in-vitro* antimicrobial activity results against the bacterial and fungal strains in the presence of metal ion than the free ligand environment. The Cu(II) complex of 4-aminoantipyrine and oxalate ion was prepared by Rajasekar<sup>86</sup> and antimicrobial activities of compounds were tested against *E. coli*, *Streptococci* and *C. albicans*.

A literature search reveals that much work has been done on the transition metal complexes of 4-aminoantipyrine derivatives, but less has been carried out on the chemistry and biological behaviour involving the amino group of 4-aminoantipyrine. It is found that less work has been carried out on the synthesis of Schiff base and its transition metal complexes involving the carbonyl group of 4-aminoantipyrine. Raman<sup>87</sup> described the synthesis, antimicrobial and DNA cleavage studies of transition metal complexes of Cu(II), Ni(II), Co(II) and Zn(II) containing Schiff base derived from salicylidene-4-aminoantipyrine and *o*-phenylenediamine. Prakash<sup>88</sup> reported synthesis and antimicrobial activity of Schiff base of 1-phenyl 2, 3-dimethyl-4-aminopyrazol-5-one (4-aminoantipyrine) and vanillin and complexes of transition metal ions. These ligand and complexes were tested for their antibacterial activity showing Zn<sup>2+</sup> and Cd<sup>2+</sup> complexes with good antibacterial activity.

It also has been observed from the results that the metal complexes have higher activity than the free ligands,<sup>89</sup> it was stated that this is probably due to the greater lipophilic nature of the complexes. Such increased activity of the metal chelates was explained on the basis of Overtone's concept and chelation theory. According to Overtone's concept of cell permeability the lipid membrane that surrounds the cell, favours the passage of lipid soluble materials, due to which liposolubility is an important factor which controls the antimicrobial activity. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of the metal ion with donor groups. Further, it increases the delocalization of electrons over the whole chelate ring and enhances the lipophilicity of the complex. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and blocks the metal binding sites on enzymes of micro-organisms. Some complexes of lanthanides (III) with 4-[(N-furfural)amino] antipyrine were prepared by Agarwal.<sup>90</sup> Transition metal complexes of Cu(II), Ni(II), Zn(II) and VO(IV), were synthesized by Raman<sup>91</sup> from the Schiff base derived from 4-

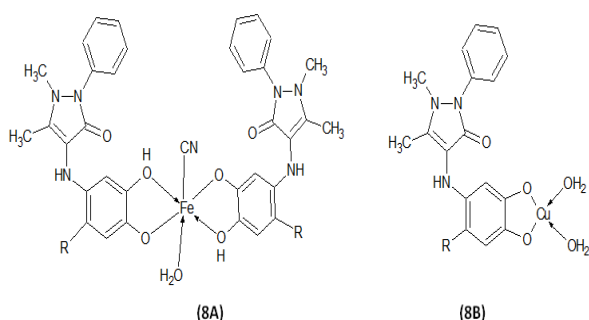
aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and acetylacetone. The antimicrobial screening tests gave good results in the presence of metal ion in the ligand system. Antony<sup>92</sup> synthesized and screened for their antimicrobial Schiff base and its 3d transition metal complexes (**7**) of Mn(II), Fe(III) and VO(IV) derived from Ethyl 4-methyl-2-oxo-6 phenylhexahydro pyrimidine-5-carboxylate and 4-aminoantipyrine suggesting possible use of the complexes as antibiotics.



(7)

A new series of transition metal complexes of Fe(III), Co(II), Cu(II) and Ni(II) was synthesized from the Schiff base ligand derived from 4-aminoantipyrine, *p*-aminoacetophenone and vanillin to give the ligand: 4-(1-(4-(hydroxy-3-methoxybenzylideneamino) phenyl) ethylideneamino)-1-pyrazol-3-one by Shareefi.<sup>93</sup>

A new series of transition metal complexes of Ni(II), Zn(II), Cd(II) and Hg(II) have been synthesized<sup>94</sup> from the Schiff base derived from dihydropyrimidine derivative of vanillin and 4-aminoantipyrine, and also screened antimicrobial potency of the ligand and complexes. The Fe(III) and Cu(II) chelates (**8A**) with coupled products (**8B**) of adrenaline hydrogen tartarate, levodopa, and carbidopa with 4-aminoantipyrine were prepared by Mohamed.<sup>95</sup>



(8A)

(8B)

The synthesis of a new series of metal complexes incorporating 4-aminoantipyrine moiety and their antimicrobial activity against the bacterial and fungal strains has been reported by Joseph.<sup>96</sup> They synthesized Cu(II) complexes from the Schiff base ligands derived from furfurylidene-4-aminoantipyrine and aniline, *p*-nitro aniline and *p*-hydroxy aniline. Tudor Rosu<sup>97</sup> have reported the synthesis of Cu(II) complexes from Schiff base ligands obtained by the condensation of 2-hydroxybenzaldehyde or terephthalic aldehyde with 4-aminoantipyrine. Raman<sup>98</sup> have reported the synthesis of Schiff bases of 4-

aminoantipyrine neutral complexes of Cu(II) from salicylidene-4-aminoantipyrine and substituted anilines. Chandra<sup>99</sup> reported antifungal and antibacterial activities of the pentadentate Schiff's base ligand 3,3'-thiodipropionic acid bis(4-amino-5-ethylimino-2,3-dimethyl-1-phenyl-3-pyrazoline) and its complexes with Co(II), Ni(II) and Cu(II) metal ions. Mishra<sup>100</sup> described the synthesis, and biological significances of VO(II), Co(II), Ni(II) and Cu(II) complexes with ligands derived from isatin-3-chloro-4-floroaniline, 2-pyridinecarboxylidene-4-aminoantipyrine exhibiting potentially useful biological activities.

Some metal complexes of oxomolybdenum (V) and dioxomolybdenum(VI) with a Schiff base derived from 4-aminoantipyrine and 2,4-dihydroxyacetophenone have been synthesized by Harikumar<sup>101</sup> antimicrobial activity of the complexes has also been examined. A new series of transition metal complexes of Cu(II), Co(II), Ni(II) and Zn(II) derived from 2-hydroxy-3-formyl-quinoline, 4-aminoantipyrine and 2-aminothiazole were synthesized<sup>102</sup> and *in-vitro* biological activities of the ligand and its complexes were tested against pathogenic bacterial and fungal strains. Metal complexes of Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) with Schiff base ligand obtained via condensation of 4-chlorobenzaldehyde and 4-aminoantipyrine prepared by Pearl<sup>103</sup> and the *in-vitro* biological screening effects of the compounds were tested against various microbial species. Metal complexes<sup>104</sup> of Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) with Schiff base ligand, via condensation of 4-chlorobenzaldimine 4-aminoantipyrine, and 2-aminophenol prepared. The *in-vitro* biological screening results show that the metal complexes are more biological active than the ligand.

Synthesis and biological activity of transition metal complexes containing a tetradentate N<sub>2</sub>O<sub>2</sub> donor type Schiff base derived from the condensation of 4-aminoantipyrine (1-phenyl-2,3-dimethyl-4-aminopyrazol-5-one) with benzyl which forms stable complexes with transition metal ions such as Cu(II), Ni(II), Co(II), Mn(II), Zn(II) and VO(IV) were reported by Raman.<sup>105</sup> Screening results indicated that the complexes show higher antimicrobial activity than the free ligand. Such increased activity of the metal chelates can be explained on the basis of Overtone's concept<sup>106</sup> and the Tweedy's chelation theory.<sup>107</sup>

## CONCLUSION

Schiff' bases and their metal complexes derived from 4-aminoantipyrine possess a number of applications. Metal complexes show greater activity than free ligands. The chemistry of Schiff bases and metal complexes is blossoming field that is being noticed. It is conceivable that the recognition of Schiff bases and metal complexes marks one of the most important milestones in human history. In addition it has provided us with tools to facilitate the search for new knowledge. This area of research has culminated in a deeper understanding of a

variety of applications including clinical, analytical, industrial and catalytical roles. By the present scenario it can be concluded that Schiff bases and their metal complexes have a great potential for further research on synthesis of novel derivatives containing these moieties which can be explored for various biological activities.

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