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An study of coordination behavior and antibacterial activities of tetradentate 2-((E)-1,5-dimethyl-2-phenyl-3-((E)-quinolin-8-methyl)-2,3-dihydro-1H-pyrazol-4-ylimino) methyl)phenol with Cu(II), Ni(II) and Co(II) metal

Amit Rai^{*1}, Ashish Kumar², Rupa Sirohi³¹Deptt.of Chemistry, Institute of Applied Medicine & Research, Ghaziabad, Jodhpur National University, Jodhpur, Rajasthan (INDIA)²Deptt.of Biotechnology, IIMT College of Medical Sciences, O Pocket Ganga Nagar, Meerut, (INDIA)³Deptt.of Biotechnology, Institute of Applied Medicine & Research, Ghaziabad, (INDIA)

E-mail : rai2878@gmail.com, dean@iamrgzb.com

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ABSTRACT

Four Schiff base metal complexes of Cu(II), Ni(II), Co(II) have been synthesized from a new tetradentate ligand, 2-((E)-1,5-dimethyl-2-phenyl-3-((E)-quinolin-8-methyl)-2,3-dihydro-1H-pyrazol-4-yliminomethyl phenol. The ligand and its complexes have been characterized on the basis of Elemental analysis, Electronic., I.R., ¹H-NMR and ¹³CNMR spectral studies. On the basis of Electronic spectral studies, for Cu (II) complex, deformed tetrahedral, Co (II) complex, tetrahedral and Ni (II) complex octahedral geometry has been proposed. The in- vitro antimicrobial activity of the investigated compounds was tested against the bacteria such as Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae and fungi Candida albicans and Rhizopus stolonifer. The data indicate that most of the metal complexes have higher antimicrobial activity than the free ligand.

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KEYWORDS

-4-amino-Antipyrine;
Metal complexes;
Antibacterial nature;
Amoxicillin.

INTRODUCTION

N-phenyl-3-substituted 5-pyrazolone derivatives are used as intermediate for the development of various anti-inflammatory agents and allergy inhibitors in pharmaceuticals^[1]. 4-amino-Antipyrine (N-phenyl-2, 3-dimethyl-4-pyrazolin-5-one) is an active moiety in the class of non-steroidal, anti-inflammatory agents used in the treatment of arthritis and other musculoskeletal and joint disorders. Some 4-amino-Antipyrine derivatives are reported to exhibit analgesic and anti-inflammatory effects.^[2], antiviral^[3] antibacterial-activities^[4].

The 4-amino-antipyrine molecule due to the presence of free -NH₂ and -C=O group can be modified into a flexible ligand system by condensation with a variety of reagents like aldehyde, ketone etc and the presence of these electron donor sites this molecule also exhibit its coordination behavior with the metal ions which contain partially filled d and f-orbital^[5-9].

In this arena, metal complexes derived from N-heterocyclic ligands, based on 4-aminoantipyrine and derivatives of aromatic amines, play an important role in pharmaceutical, clinical and analytical applications and their complexes with platinum (II) and cobalt (II) ions

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have been shown to acts as antitumor substances^[10].

Herein we report the synthesis of a novel Schiff base ligand, 2-((E)-1,5-dimethyl-2-phenyl-3-((E)-quinolin-8-methyl)-2,3-dihydro-1H-pyrazol-4-ylimino)methyl)phenol (DPQDPP) derived from 4-amino-Antipyrine, salicyclic aldehyde and 8-amino-quinoline and it's Cu (II), Co (II) and Ni (II) complexes. Their spectral properties and antibacterial nature were investigated against bacteria as (*E. coli*, *S. aureus* and *K. pneumoniae*) and fungi (*C. Albicans* and *R. stolonifer*)

MATERIALS

All chemicals used in this work were grade of BDH or Aldrich including NH_4OH , CHCl_3 , $\text{C}_2\text{H}_5\text{OH}$, DMF NaOH, Salicyc aldehyde and Tryptophan (α -amino-1-indole propionic acid). The organic Schiff base ligands and 2, 3-dimethyl-1-phenyl-4-salicyclidene -3-pyrazolin-5-one was reported earlier^[11-13].

Double distilled water were used throughout the experiment. Which show its neutral P^{H} and zero conductivity.

Synthesis of ligand

The ethanolic solution of salicylidene-4-aminoantipyrine (10 m mole) was refluxed with 8-amino-quinoline (10 m mole) for 10 hrs in presence of K_2CO_3 . After refluxing, the volume of the solution was reduced to one third. On cooling, a dark brown solid was separated, filtered and recrystallized from ethanol. Salicylidene-4-aminoantipyrine Schiff base was prepared as reported in the literature^[14-16].

Synthesis of metal complexes

An ethanolic solution of the ligand (DPQDPP) (10 m mole) was refluxed with (10 m mole) Metal chloride [(Co (II), Cu (II) and Ni (II) for ca. 4 hrs. The mixture was kept at 0°C for ca. 12 hrs. The solid product so formed was separated by filtration and washed thoroughly with hot ethanol and then dried in vacuo. Yield: 60%

Bacterial culture

The strains of bacteria used were *E. Coli*, *S. aureus* and *K. pneumoniae* and fungi *C. albicans* and *R. stolonifer*. All strains were isolated from patients in

L.L.R. medical college hospital. The identity of all strains was confirmed. A bacterial pension was prepared and added to the sterilized medium before solidification. The media with bacteria was poured in to sterilized Petri dishes under aseptic condition. 5 mg weights of Schiff base, and Co(II), Ni(II) and Cu(II) complexes of Schiff base complexes were placed on the surface of the culture and incubated at 37°C for 24 hours. After incubation the inhibition (mm) and average of inhibition zones recorded.

RESULTS AND DISCUSSION

All the complexes are air stable. They were identified by their physical and analytical data. The monomeric nature of the complexes was evidenced from their magnetic susceptibility values (TABLE 1). Study of magnetic and electronic spectral data is quite informative in characterizing the geometry of the complexes. These complexes were non-electrolytic due to the low conductivity values^[17].

TABLE 1 : Microanalysis of Ligand and Metal complexes

Ligand/ Metal complexes	C%	H%	N%	Metal%	Molar conduc tivity	μ_{eff} B.M.
	calc./ found	calc./ found	calc./ found	calc./ found	$\text{Ohm}^{-1}\text{cm}^2$ mol^{-1}	
$\text{C}_{30}\text{H}_{30}\text{N}_5\text{O}$ (DPQDPP)	75.60/ 75.55	6.34/ 6.35	14.69/ 14.59	--	--	
[Cu(DPQDPP)]	66.83/ 66.85	5.42/ 5.40	12.99/ 12.85	11.79/ 11.85	08	4.95
[Co(DPQDPP)]	67.41/ 67.48	5.47/ 5.49	13.10/ 13.05	11.03/ 11.00	07	3.52
[Ni(DPQDPP)]	67.44/ 67.88	5.47/ 5.40	13.11/ 13.05	10.99/ 11.93	05	1.91

Electronic absorption spectra

The electronic absorption spectra of the ligand and its complexes were recorded at 300 K in DMSO solution. Electronic spectra of Cu (II) complex present two type of $d \rightarrow d$ transition $xy \rightarrow xz$, yz and $xy \rightarrow z^2$, x^2-y^2 at 14650 cm^{-1} whose values are characteristics of a deformed tetrahedral geometry. The Co(II) complex also exhibit $d \rightarrow d$ transition $xy \rightarrow xz$, yz a at 9746 cm^{-1} and $xy \rightarrow z^2$, x^2-y^2 at 15247 cm^{-1} and characteristics of a tetragonal geometry. The absorption spectra of Ni (II) complex display three $d \rightarrow d$ transitions $z^2 \rightarrow x^2-y^2$,

$xy \rightarrow x^2-y^2$ and $xy.yz \rightarrow x^2-y^2$ in the range of 11135-121081 cm^{-1} , 8621-19416 cm^{-1} and 21413-27322 cm^{-1} proposed octahedral geometry. TABLE 3 show Electronic absorption spectral data of the complexes.

TABLE 3 : Electronic spectral data of Ligand and Metal complexes

Metal Complexes	Transition	Geometry
[Cu(DPQDPP)]	$xy \rightarrow xy \rightarrow z^2, x^2 - y^2$	Deformed tetrahedral
[Co(DPQDPP)]	$xy \rightarrow xy \rightarrow z^2, x^2 - y^2$	Tetragonal
[Ni (DPQDPP)]	$z^2 \rightarrow x^2 - y^2$ $xy \rightarrow x^2 - y^2$	octahedral

IR spectra

The spectrum of the ligand shows a weak broad band in the region 3000-3200 cm^{-1} assignable to intramolecular hydrogen bonded -OH groups^[18]. The absence of this band, noted in the spectra of the complexes, indicates the deprotonation of the -OH group on complexation. The spectra of the ligand shows a characteristic -C=N bands in the region 1610 cm^{-1} which are also shifted to lower frequencies in the spectra of the complexes (1580 cm^{-1}). The bands in the ligand spectrum at 1560 cm^{-1} and 1410 cm^{-1} are ascribed to C=N and C=C of quinilone ring, but there is no appreciable change in the complex spectrum which indicates that quinolonic nitrogen atom does not involve in the coordination. The IR spectra of the metal chelates also show some new bands in the region 460-450 cm^{-1} and 400-380 cm^{-1} which are probably due to the formation of (M-O) and (M-N) bonds respectively. All complexes show specific band ν (C=O) band (cyclic keto group present in the pyrazole ring at 1615, 1596 cm^{-1}) moves towards lower wave length (1589, 1580 cm^{-1}) suggesting the coordination of the ligands to the metallic ion via carbonyl group^[19,20].

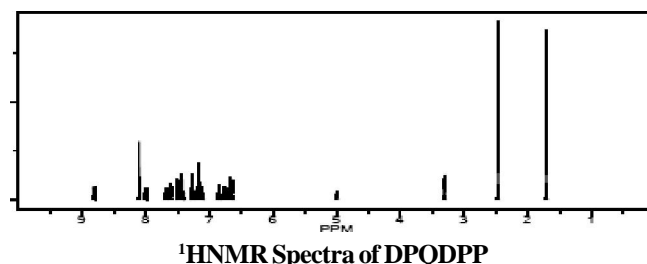
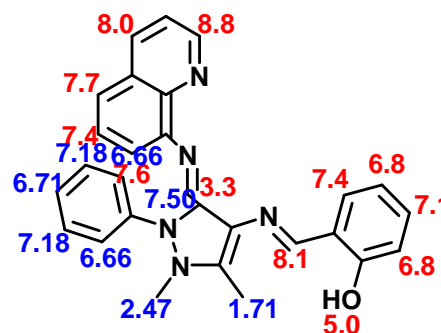
¹H-NMR

The ¹H-NMR spectrum of the ligand in DMSO-*d*₆ shows the following signals; C₆H₅ as a multiplet around 6.8-7.4 δ , -C-CH₃ at 1.71 δ , -N-CH₃ at 2.47. The spectra of ligand show singlet at δ 8.5 due to azomethine proton at 8.5 δ . The peak at 6.66-8.8 δ is attributed to quinoline moiety^[25]. The peaks at δ 5.0 are attributed to the phenolic -OH group present in the salicylaldehyde

TABLE 2 : Infrared Spectral Frequencies of Ligand and Metal complexes

Ligand/Schiff base	$\nu(\text{OH})$ cm^{-1}	$\nu(\text{C=O})$ cm^{-1}	$\nu(\text{C=N})$ cm^{-1}	$\nu(\text{N-N})$ cm^{-1}	$\nu(\text{M-O})$ cm^{-1}	$\nu(\text{M-N})$ cm^{-1}
DPQDPP	3200 m	1605s	1610br	1034m	460s	400m
[Cu(DPQDPP)]	-	1604 mw	1580 mw	1035 mw	458br	390 br
[Co(DPQDPP)]	-	1606br	1605 m	1030 mw	455 br	380mw
[Ni(DPQDPP)]	-	1608 mw	1600mw	1033 m	450	385 m

moiety and This peak is absent in the metal complexes confirming the loss of -OH protons due to complexation^[26-28].



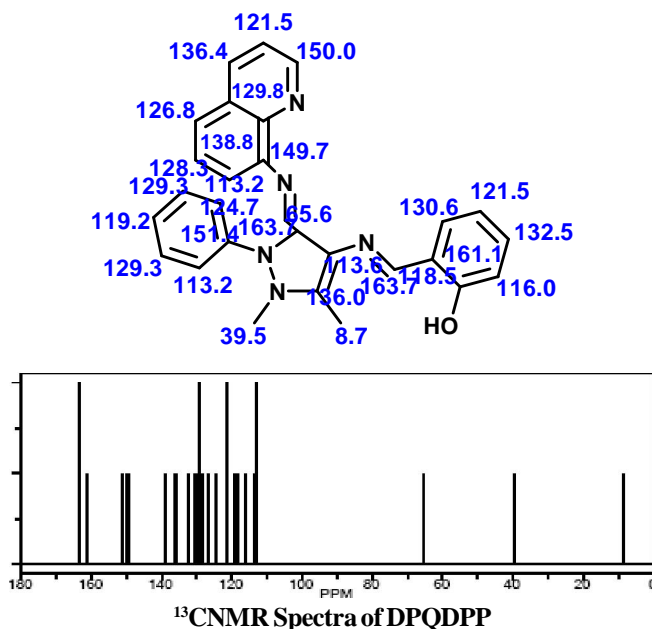
¹³C-NMR

The spectra display the signals corresponding to different nonequivalent carbon atom at δ 8.8 ppm (-C-CH₃), 39.6 (-N-CH₃) corresponding to carbon atom of methyl group at ca. δ 150 ppm (C=N) due to carbon atom of azomethine group and δ 150, 121.5, 136.4, 129.0, 126.8, 138.8, 129.8, 126.8, 138.8, 149.7 due to aromatic carbon atom of quinolonic ring^[29-31].

Antimicrobial activity

The *in vitro* antimicrobial activity of the investigated compounds was tested against the bacteria such as *S. aureus*, *E. coli*, *K. pneumoniae* and also fungi *C. albicans*

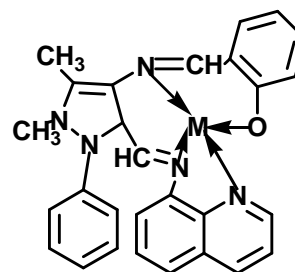
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and *R. stolonifer* by the serial dilution method. The minimum inhibitory concentration (MIC) values of the compounds against the growth of microorganisms are summarized in TABLE 4. A comparative study of the ligand and its complexes (MIC values) indicates that the complexes exhibit slightly higher antimicrobial activity than the free ligand. Such increased activity of the complexes can be explained on the basis of Overtones concept^[31] and Tweedys Chelation theory^[32]. According to Overtones concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only the 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 the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of the proteins that restricts further growth of the organism. Furthermore, the mode of action of the compound may involve formation of a hydrogen bond through the azomethine group with the active centre of cell constituents, resulting in interference with normal cell process.

TABLE 4 : Antimicrobial study of the investigated compounds (MIC X 10⁻²M)

Compound	<i>E. coli</i>	<i>S.aureus</i>	<i>K.pneu moniae</i>	<i>C.albi cans</i>	<i>R.sto lonifer</i>
DPQDPP	4.8	4.2	5.6	3.8	5.9
[Cu(DPQDPP)]	3.2	2.5	3.2	2.9	4.4
[Co(DPQDPP)]	4.1	3.2	4.9	2.1	5.1
[Ni(DPQDPP)]	2.8	2.9	3.5	3.1	3.9
Amoxicillin	2.1	4.0	4.9	3.0	5.2



CONCLUSION

The following structure of metal complexes are proposed.

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