

# SYNTHESIS AND CHARACTERIZATION OF TRANSITION METAL COMPLEXES OF NOVEL SCHIFF BASE 8-[(Z)-{[3-(N-METHYLAMINO) PROPYL] IMINO}METHYL]-7-HYDROXY-4-METHYL-2H-CHROMEN-2-ONE][NMAPIMHMC] AND THEIR BIOLOGICAL ACTIVITIES

Sudhir S. Sawant<sup>1\*</sup>, Vijaya Pawar<sup>2</sup>, Shirish Janrao<sup>3</sup>, Ramesh S. Yamgar<sup>2</sup> and Y. Nivid

<sup>1</sup>P. G. Dept of Chemistry, Govt. of Maharashtra's Ismail Yusuf College of Arts, Science and Commerce, Jogeshwari (East), Mumbai- 400 060 India.

<sup>2</sup>Department of Chemistry, Patkar College of Arts and Science, Goregaon (W), Mumbai- 400 062, India.

<sup>3</sup>Bio-Analytical Technology ( India) Pvt. Ltd., B.A.T. House, Plot no.985, 720/10, Navi Peth, Off Lal Bahadur Shastri Road, Pune, Maharashtra-411 030, India.

## ABSTRACT

This paper presents the structure and antibacterial properties of some complexes of Co(II), Ni(II), Cu(II), and Zn(II), with a novel Schiff base obtained from 4-Methyl 7-hydroxy 8-formyl coumarin, and N-methylamino propylene diamine. The Schiff base was characterized by physical, spectral and analytical data. The synthesized Schiff base act as bidentate ligand for the complexation reaction with Cu(II), Ni(II), Co(II) and Zn(II) ions. The structure of each complex was characterized by spectroscopic methods (IR, UV-Vis, <sup>1</sup>H-NMR, and Mass spectroscopy) and elemental analysis. Molecular weight of few metal complexes was confirmed by high resolution mass spectroscopy. According to these data, we propose an octahedral geometry for Co(II), Ni(II), Zn(II) and Cu(II) complexes. Antibacterial activity of the ligand and its complexes were tested against selected bacteria. The ligand and all the complexes possess antimicrobial and antifungal activity. The transition metal complexes have shown superior antimicrobial and antifungal activities as compared to Schiff base ligand.

**Keywords:** 4-Methyl 7-hydroxy 8-formyl coumarin, N-methylamino propylene diamine.

## INTRODUCTION

Synthesis and characterization of transition metal complexes containing Schiff bases as ligands has been a topic of interest to researchers due to their importance as catalysts in many reactions<sup>1-6</sup>. These ligand

systems have evoked considerable interest because of their utility as model compounds in bioinorganic studies<sup>7-9</sup>. Schiff bases form an important class of organic compounds in chemistry due to their useful physical and chemical properties and large number of

reactions they undergo. They are also having wide industrial applications and very interesting biological and pharmacological activities. Schiff bases derived from substituted aliphatic amines and aromatic aldehydes have a wide variety of applications in many fields, e.g. biological, inorganic and analytical chemistry<sup>10-14</sup>. Currently, there is a revival of interest in bioactive natural products as chemical lead compounds for the generation of semi-synthetic derivatives. Recent research has shown that metal complexes based on natural products afforded a novel approach to a potential pro-drug<sup>15-17</sup>. Schiff bases and their metal complexes are known to exhibit anticancer, antioxidant and anti-inflammatory activities<sup>18-22</sup>. In this paper we report the synthesis and characterization of novel Schiff base derived from 4-Methyl-7-hydroxy-8-formyl coumarin i.e. 8-[(Z)-{[3-(N-methylamino)propyl]imino}methyl]-7-hydroxy-4-methyl-2H-chromen-2-one [NMAPIMHMC] and its transition metal complexes and their antimicrobial properties.

## EXPERIMENTAL

### Material and Methods

All chemicals and solvents used were of LR grade. All metal(II) chloride salts were used. The proton magnetic spectra were recorded on a Bruker AMX-5000 Spectrometer. Mass spectra were recorded on Mass spectrophotometer AB Sciex API-4000. IR spectra were recorded on a Jasco FTIR Spectrophotometer. UV-Visible spectra were obtained in DMF on a Shimadzu UV-Visible Spectrophotometer.

### Synthesis of 4-Methyl 7-hydroxy coumarin

4-Methyl 7-hydroxy coumarin was prepared by the reported method<sup>23</sup>. Concentrated H<sub>2</sub>SO<sub>4</sub> (500 ml) was cooled to 0<sup>o</sup> C in ice bath. Mixture of ethylacetoacetate (65 ml) and meta-Cresol (55 ml) was added in concentrated H<sub>2</sub>SO<sub>4</sub> under vigorous stirring at 0-5<sup>o</sup> C over a period of 1-1.5 hrs. Stirring was continued at 5<sup>o</sup> C for 2 hrs. Temperature of reaction mixture was then raised slowly to 30<sup>o</sup> C and allowed to stand for 24 hrs. The solution was then poured in ice bath and water. The product precipitated was filtered. The crude product was dissolved in 5% NaOH solution and the solution was then clarified with activated charcoal and filtered. Filtrate was acidified with conc. HCl to give 4-Methyl 7-hydroxyl coumarin. The yield of the product was around 95%.

### Synthesis of 4-methyl-7-hydroxy 8-formyl coumarin<sup>24</sup>

4-Methyl 7-hydroxy coumarin (30g, 0.170 moles) was dissolved in 300 ml glacial acetic acid. Hexamine (60 g, 0.428 moles) was added and heated to 85-90<sup>o</sup> C for 5 hours. Reaction was monitored by TLC (30% Ethyl acetate in hexane). After reaction was completed, as indicated by TLC, Reaction mixture was quenched in 20% HCl and heated to 60-80<sup>o</sup> C for 20 minutes. Reaction mixture was cooled to room temperature and product was extracted in methylene chloride (100 ml x 3 times). Combined MDC extract was washed with distilled water and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. MDC extract was concentrated and crude product was purified by Silica gel column chromatography to get pure 4-Methyl-7-hydroxy-8-formyl coumarin. The yield of the product was around 20%.

### Synthesis of Schiff base

The Schiff base i.e. the ligand 8-[(Z)-{[3-(N-methylamino)propyl]imino}methyl]-7-hydroxy-4-methyl-2H-chromen-2-one [NMAPIMHMC] was synthesized by the condensation of 8-Formyl-7-Hydroxy-4-Methylcoumarin with N-methylpropane-1,3-diamine in (1:1) molar proportion in ethanol in the presence of traces of concentrated hydrochloric acid. The reaction mixture was refluxed for an hour. On cooling, the product was isolated to obtained yellowish brown oily mass of the schiff base.

As the schiff base was an oily mass and unstable in nature, it was difficult to characterize the compound. Therefore, its oxalate salt was prepared for spectral characterization.

The Schiff base 8-[(Z)-{[3-(N-methylamino)propyl]imino}methyl]-7-hydroxy-4-methyl-2H-chromen-2-one [NMAPIMHMC] was obtained by the reaction of N-methylpropane-1,3-diamine with 4-methyl-7-hydroxy 8-formyl coumarin in (1:1) molar proportion in ethanol in the presence of traces of concentrated hydrochloric acid. The reaction mixture was refluxed for an hour. It was then treated with Oxalic acid (1 mole equivalent) and further refluxed for an hour. On cooling, the product was isolated as yellow coloured oxalate salt which was recrystallized from alcohol. The yield of the product was around 70%. M.P. 199<sup>o</sup> C, <sup>1</sup>H NMR DMSO(d<sub>6</sub>) 90MHz, δ<sub>H</sub> 1.62-1.63(m, 2H), 2.11(m, 2H), 2.51(s, 3H), 3.02(t, 2H), 5.15(s, 1H), 5.97(d, 2H, J=9.3Hz), 6.94(d, J=9.3Hz) 8.17(s, 1H). MS : [M+1]<sup>+</sup> 275.3. IR : ν<sub>N-H</sub> 3460 cm<sup>-1</sup>, ν<sub>C=O</sub> (Lacton) 1718 cm<sup>-1</sup>, ν<sub>C=N</sub> 1603 cm<sup>-1</sup>, ν<sub>C-O-C</sub> 1079 cm<sup>-1</sup>, Phenolic ν<sub>C-O</sub> 1310 cm<sup>-1</sup>.

UV:  $\lambda_{\max}$  225 nm, 313 nm

### Synthesis of Metal Complexes of Schiff base

As the Schiff base [NMAPIMHMC] was an oily product, it was freshly prepared *in situ* by mixing *N*-methylpropane-1,3-diamine with 4-methyl-7-hydroxy 8-formyl coumarin in (1:1) molar proportion in ethanol. Then equimolar quantities of divalent metal chloride were mixed and the reaction mixture was heated on water bath for about five hours. It was then cooled and pH was adjusted to about 8.5 by 25% aq. ammonia when coloured solid separated out which was filtered and washed with ethanol, recrystallized in ethanol and dried in oven at 80-100°C. This is the general method for the synthesis of metal complexes of ligand with divalent metal chlorides  $MCl_2 \cdot 2H_2O$  Where M= Co(II), Ni(II), Cu(II), Zn(II). Since Zn (NMAPIMHMC) $_2 \cdot 2H_2O$  Complex was diamagnetic in nature, it could be scanned for  $^1H$  NMR in DMSO( $d_6$ ) 700MHz,  $\delta_H$  2.06(m, 2H), 2.34(s,3H), 2.96( t, 2H), 3.73( t, 2H), 5.98(s, 1H), 6.56( d, 2H, J=8.4Hz), 7.56(d, J=8.4Hz) 8.83(s, 1H).

## RESULTS AND DISCUSSION

### Physical properties

The Schiff base [NMAPIMHMC] (Fig. 1) was freshly prepared by refluxing *N*-methylpropane-1,3-diamine with 4-methyl-7-hydroxy 8-formyl coumarin in (1:1) molar proportion in ethanol in the presence of traces of concentrated hydrochloric acid.

This Schiff base was then used for the complexation with Cu(II),Co(II), Ni(II), and Zn(II) ions. All of the synthesized metal complexes were air and moisture stable. These were prepared by the stoichiometric reaction of the corresponding metal salts ( as chlorides) and the Schiff base in molar ratios M:L of 1:2. The complexes are intensely colored, which decomposes above 250°C. They are insoluble in common organic solvents such as chloroform or acetone, slightly soluble in ethanol, methanol, but soluble in DMSO and DMF. [ Figure 1]

### Infrared spectra

IR spectra of the Schiff base oxalate salt showed the absence of bands at 1725 and 3300  $cm^{-1}$  due to carbonyl  $\nu(C=O)$  and  $\nu(NH_2)$  stretching vibrations and, instead, appearance of a strong new band at  $\sim 1630$   $cm^{-1}$  assigned<sup>25</sup> to the azomethine,  $\nu(C=N)$  linkage. It suggested that amino and aldehyde moieties of the starting reagents are absent and have been converted into the azomethine moiety

(Fig.1). The comparison of the IR spectra of the Schiff base and their metal complexes (Table 1 & 2) indicated that the Schiff base was principally coordinated to the metal atom

1. The band appearing at 1610  $cm^{-1}$  due to the azomethine was shifted to lower frequency by  $\sim 10-20$   $cm^{-1}$  indicating<sup>[26]</sup> participation of the azomethine nitrogen in the complexation.
2. A band appearing at 3371-3119  $cm^{-1}$  in metal complexes which have significantly different characteristic of  $\nu_{OH}$  stretching vibration due to stretching modes of coordinated water molecule.
3. Further conclusive evidence of the coordination of these Schiff base compounds with the metals, was shown by the appearance of weak low frequency new bands at 545-559 and 450-453  $cm^{-1}$ . These were assigned<sup>27,28</sup> to the metal-nitrogen (M-N) and metal-oxygen (M-O) respectively. These new bands were observed in the spectra of the metal complexes and not in the spectra of its Schiff base compounds thus confirming participation of these hetero groups (O and N) in the coordination.

### $^1H$ NMR spectra<sup>29</sup>

The proton magnetic resonance spectrum of Schiff base (NMAPIMHMC) in DMSO solution shows a N=CH azomethine proton at  $\delta$  8.17 and methyl protons of 8-Formyl-7-Hydroxy-4-Methylcoumarin at  $\delta$  2.51. Comparative assignment values are shown in Table 3. Due to its diamagnetic nature metal complex Zn (NMAPIMHMC) $_2 \cdot 2H_2O$ ,  $^1H$  NMR spectrum was scanned in DMSO- $d_6$ . It was observed that the azomethine proton at 10.59 ppm in 8-Formyl-7-Hydroxy-4-Methylcoumarin was appearing at 8.17ppm in schiff's base. After complexation with Zinc metal it was shifted significantly downfield to 8.83ppm due to deshielding effect exerted by metal atom. Apart from the downfield shift of azomethine, following other interesting observations were also made. Aromatic protons of coumarin ring appearing at 5.87 ppm and 6.84 ppm in schiff's base were shifted to 6.56ppm and 7.56 ppm respectively due to the electron withdrawing mesomeric effect exerted by Zinc metal atom. Olefinic proton of coumarin ring appearing at 5.24 ppm was also shifted down field to 5.98 ppm due to electron withdrawing mesomeric effect operating through the conjugation across the aromatic ring over the

$\alpha,\beta$ -unsaturated double bond of coumarin ring. The methyl protons and phenyl protons of Schiff base of the divalent metal ion complexes of both ligands are showing shift in  $\delta$  values.

### $^{13}\text{C}$ NMR<sup>29</sup>

Carbon atom positions obtained are compared with known compound 8-Acetyl-7-hydroxy-4-methyl coumarin having similar structure to that of 8-formyl-7-hydroxy-4-methyl coumarin. Comparative assignment values are shown in [Figure 2] and [Table 4].

### Mass spectra

High resolution mass spectra of Schiff's base NMAPIMHMC. Oxalate salt showed  $[\text{M}+1]^+$  at 275.4 thus confirming formation of Schiff base. Mass spectra of  $\text{Cu}(\text{NMAPIMHMC})_2 \cdot 2\text{H}_2\text{O}$  showed  $[\text{M}+1]^+$  at 611 and  $[\text{M}-\text{L}]^+$  at 336. Mass spectra of  $\text{Ni}(\text{NMAPIMHMC})_2 \cdot 2\text{H}_2\text{O}$  showed  $[\text{M}-\text{L} + \text{H}_2\text{O}]^+$  at 349 and  $[\text{M}-\text{L}]^+$  at 331. Mass spectra of  $\text{Zn}(\text{NMAPIMHMC})_2 \cdot 2\text{H}_2\text{O}$  showed  $[\text{M}+1]^+$  at 612 and  $[\text{M}-\text{L} + \text{H}_2\text{O}]^+$  at 356 and  $[\text{M}-\text{L}]^+$  338. Mass spectrum of  $\text{Co}(\text{NMAPIMHMC})_2 \cdot 2\text{H}_2\text{O}$  showed  $[\text{M}+1]^+$  at 606 and  $[\text{M}-\text{L}]^+$  at 331. [ Figure 3 & Figure 4] [Table 5]

From the discussion of the results of various spectroscopic details presented above, it may be concluded that the proposed geometry for the transition metal complexes with general formula  $\text{ML}_2 \cdot 2\text{H}_2\text{O}$  is octahedral for  $\text{Co}(\text{II}), \text{Ni}(\text{II}), \text{Zn}(\text{II})$  complexes and for  $\text{ML}_2$  is square planer for  $\text{Cu}(\text{II})$  complexes and the bonding in the complexes can be represented as follows:[Figure 5]

### Antimicrobial properties

Schiff base and transition metal chelates were evaluated for their antibacterial activity against the strains Gram-negative bacteria viz. *Escherichia coli* and antifungal activity against strain *Aspergillus niger* by the tube dilution technique.

The lowest concentration which showed no visible growth was taken as an end point known as minimum inhibitory concentration (MIC).

A comparison of the antimicrobial activity of the Schiff base and their metal complexes shows that the antimicrobial activity of the

Schiff base was enhanced due to the complexation with metal ion. The results of the studies of minimum inhibitory concentration of the Schiff base and their metal complexes are summarized in (Table 6).

### CONCLUSION

Novel Schiff base 8-[(Z)-{3-(N-methylamino)propyl}imino}methyl]-7-hydroxy-4-methyl-2H-chromen-2-one] [NMAPIMHMC] was obtained by the reaction of *N*-methylpropane-1,3-diamine with 4-methyl-7-hydroxy 8-formyl coumarin and characterised by  $^1\text{H}$ NMR,  $^{13}\text{C}$ NMR and HRMS techniques. Novel transition metal complexes with  $\text{Co}(\text{II}), \text{Ni}(\text{II}), \text{Cu}(\text{II})$  and  $\text{Zn}(\text{II})$  were prepared, characterised and their antibacterial and antifungal activity was screened.

In the antibacterial screening against bacteria *Escherichia coli* it was found that the ligands show MIC values greater than 200  $\mu\text{g}/\text{ml}$ , whereas transition metal complexes of ligands showed MIC values less than 20  $\mu\text{g}/\text{ml}$ . Hence it can be concluded that Metal complexes of transition metals of the ligand have better activity against *Escherichia coli*.

Antifungal screening was done against organism such as *Aspergillus niger*, the ligands show MIC values less than 200  $\mu\text{g}/\text{ml}$ , whereas transition metal complexes of the ligand showed MIC values less than 20  $\mu\text{g}/\text{ml}$ . Hence it can be concluded that transition metal complexes of the ligand showed better activity against *Aspergillus niger*.

The results of the screening of the Schiff base and transition metal complexes for antimicrobial activity indicate that the antimicrobial activity of the Schiff base was enhanced on complex formation with metal in all cases studied.

**Note:** Authors have no conflict of interest.

### ACKNOWLEDGEMENTS

The authors gratefully acknowledge NMR facility of TIFR, Mumbai for  $^1\text{H}$  &  $^{13}\text{C}$  NMR spectra. We are also grateful to the Principal of Patkar-Varde College, Goregaon Mumbai and Principal of Ismail Yusuf College, Jogeshwari, Mumbai for guidance, constant encouragement and support to carry out this research work.

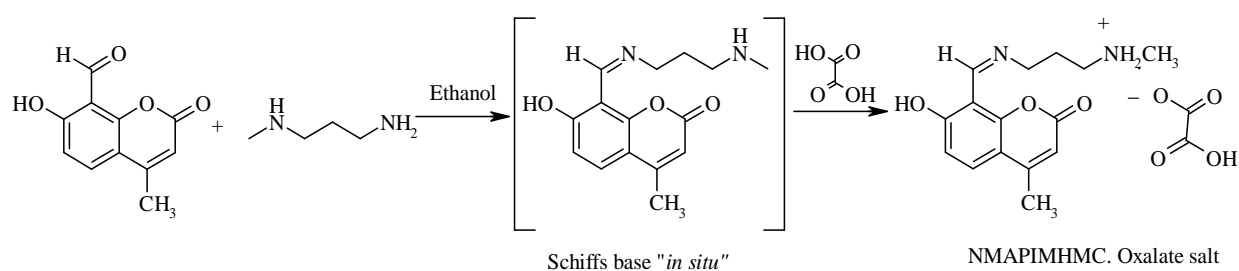


Fig. 1: Synthetic scheme for NMAPIMHMC( in situ) and its oxalate salt

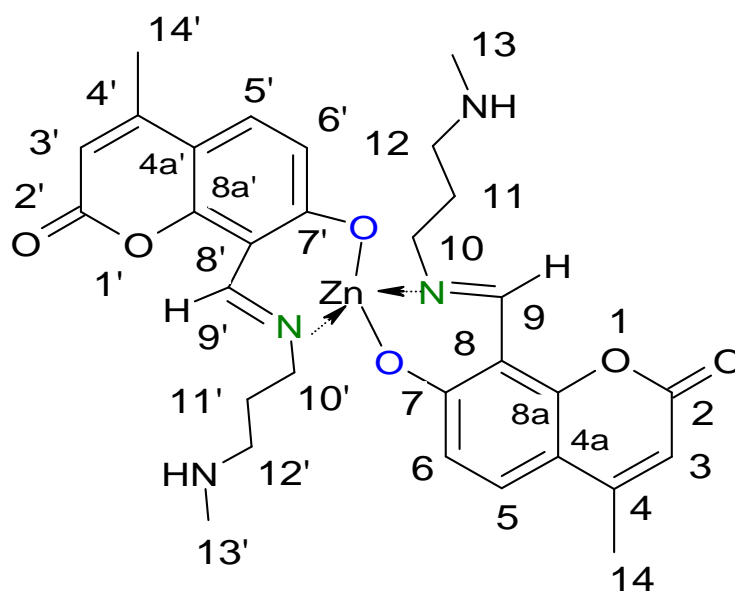


Fig. 2: Atom numbering of  $Zn[NMAPIMHMC]_2 \cdot 2H_2O$  complex

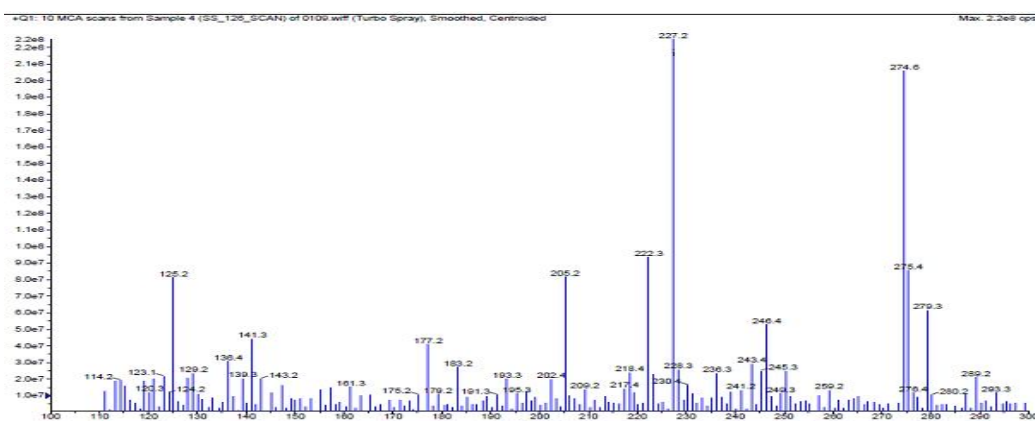


Fig. 3 Mass spectrum of  $Co(NMAPIMHMC)_2 \cdot 2H_2O$  complex

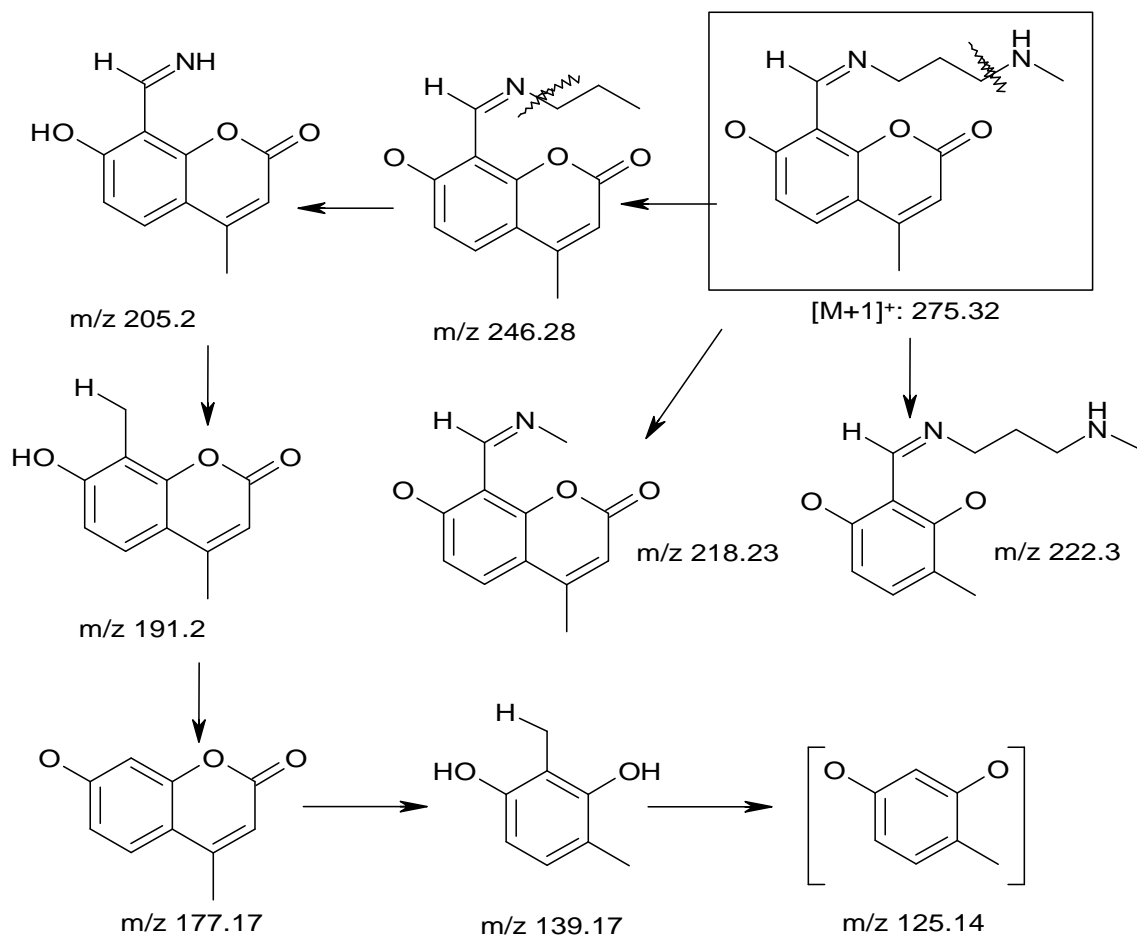


Fig. 4 Mass fragments of Schiff's base NMAPIMHMC. Oxalate salt

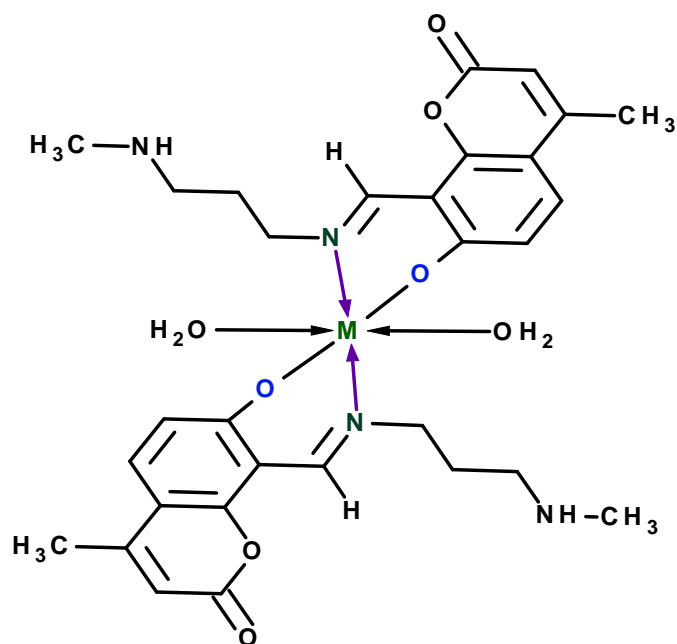


Fig. 5: Proposed structure of  $M(NMAPIMHMC)_2 \cdot 2H_2O$  complexes, Where M is divalent metal atom like Cu, Co, Ni and Zn



**Table 1: Infrared Spectral Data (cm<sup>-1</sup>) of the Schiff base Ligand (NMAPIMHMC).Oxalate salt**

Schiff base Ligand	$\nu_{N-H}$	$\nu_{C=N}$	$\nu_{C=O}$ Lactonyl	Phenolic c-o
NMAPIMHMC	3468	1610	1715	1313

**Table 2: FT-IR Bands for Metal Complexes of (NMAPIMHMC) and their Assignments**

Complex	Lattice water $\nu$ (OH) cm <sup>-1</sup>	Lactonyl $\nu$ C=O cm <sup>-1</sup>	$\nu$ C=N cm <sup>-1</sup>	Phenolic C-O cm <sup>-1</sup>	$\nu$ M-N cm <sup>-1</sup>	$\nu$ M-O cm <sup>-1</sup>
Co[(NMAPIMHMC) <sub>2</sub> ].2H <sub>2</sub> O	3371	1716	1615	1395	554	450
Ni[(NMAPIMHMC) <sub>2</sub> ].2H <sub>2</sub> O	3372	1719	1631	1406	559	450
Cu (NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	3212	1717	1631	1412	545	451
Zn (NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	3119	1728	1631	1411	550	453

**Table 3: <sup>1</sup>H NMR assignments of Schiff base NMAPIMHMC & Zn(NMAPIMHMC)<sub>2</sub>.2H<sub>2</sub>O metal complex**

$\delta$ value in ppm Schiff base NMAPIMHMC	$\delta$ value in ppm Metal complex Zn(NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	Multiplicity & Number of Protons	Assignment
1.62-1.63	2.06	m (2H)	C-CH <sub>2</sub> -C
2.11	2.34	s (3H)	-N-CH <sub>3</sub>
2.41	2.51	s (3H)	=C-CH <sub>3</sub>
2.75	2.96	t (2H)	N-CH <sub>2</sub>
3.02	3.73	t (2H)	=N-CH <sub>2</sub>
5.15	5.98	s (1H)	=C-H olefinic
5.97	6.56	d (2H)	
6.94	7.56	d (2H)	
8.17	8.83	s (1H)	=N-H Azomethine

**Table 4: <sup>13</sup>C NMR assignments of Zn (NMAPIMHMC)<sub>2</sub>.2H<sub>2</sub>O metal complex**

Atom No.	Group	<sup>13</sup> C ppm	8-Acetyl-7-hydroxy- 4-methylcoumarin
2, 2'	C	162.733	162.0
3, 3'	CH	107.248	112.5
4, 4'	C	106.985	152.8
4a, 4a'	C	106.322	113.6
5, 5'	CH	130.107	132.6
6, 6'	CH	120.355	112.5
7, 7'	C	154.867	160.3
8, 8'	C	156.861	117.4
8a, 8a'	C	160.229	149.3
9, 9'	C	173.636	199.8
10, 10'	CH <sub>2</sub>	58.48	na
11, 11'	CH <sub>2</sub>	33.582	na
12, 12'	CH <sub>2</sub>	47.342	na
13, 13'	CH <sub>3</sub>	27.064	na
14, 14'	CH <sub>3</sub>	18.892	21.2

**Table 5: Mass Spectral Data for the Metal Complexes**

Complex	Fragments m/z
Cu(NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	[M+1] <sup>+</sup> 611, [M-L +H <sub>2</sub> O] 354, [M-L] <sup>+</sup> 336.
Ni(NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	[M-L +H <sub>2</sub> O] 349, [M-L] <sup>+</sup> 331.
Zn(NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	[M+1] <sup>+</sup> 612, [M-L +H <sub>2</sub> O] 356, [M-L] <sup>+</sup> 338.
Co(NMAPIMHMC) <sub>2</sub> .2H <sub>2</sub> O	[M+1] <sup>+</sup> 606, [M-L] <sup>+</sup> 331.

**Table 6: Antimicrobial Activity (MIC,  $\mu\text{g ml}^{-1}$ ) of Schiff base [NMAPIMHMC] and its Metal Complexes**

Compound	<i>Escherichia coli</i>	<i>Aspergillus niger</i>
[NMAPIMHMC]	<200	<200
$\text{Co}[\text{NMAPIMHMC}]_2 \cdot 2\text{H}_2\text{O}$	<20	<20
$\text{Ni}[\text{NMAPIMHMC}]_2 \cdot 2\text{H}_2\text{O}$	<20	<20
$\text{Cu}[\text{NMAPIMHMC}]_2 \cdot 2\text{H}_2\text{O}$	<20	<20
$\text{Zn}[\text{NMAPIMHMC}]_2 \cdot 2\text{H}_2\text{O}$	<20	<20

## REFERENCES

- Singh DP, Kumar R, Mehani R and Verma SK. Synthesis and characterization of divalent metal complexes with ligand derived from the reaction of 4-aminopyridine and biacetyl. *J Serb Chem Soc.* 2006;71:939.
- Deepa K, Madhu NT, Radhakrishnan PK. Metal complexes of schiff bases derived from dicinnamoylmethane and aromatic amines, *Synth. React. Inorg. Met.-Org. Chem.* 2005;35: 883.
- Chohan ZH, Pervez H, Rauf A, Khan KM, Supuran CT. Isatin-derived Antibacterial and Antifungal Compounds and their Transition Metal Complexes. *J Enzyme Inhib. Med Chem.* 2004;19:417.
- Karvembu R and Natarajan K. Synthesis and spectral studies of binuclear ruthenium(II) carbonyl complexes containing bis( $\beta$ -diketone) and their applications, *Polyhedron.* 2002;21: 219.
- Ali SA, Soliman AA, Aboaly MM, Ramadan RM. Chromium, Molybdenum and Ruthenium Complexes of 2-Hydroxyacetophenone Schiff Bases. *J Coord Chem.* 2002;55:1161.
- Chatterjee D, Mitra A and Roy BC. Oxidation of organic substrates catalyzed by a novel mixed-ligand ruthenium(III) complex. *J Mol Cat.* 2000;161:17.
- Alaudeen M, Abraham A, Radhakrishnan PK. Synthesis and antibacterial activity of rare earth perchlorate complexes of 4-(2'-hydroxynaphthylazo)antipyrine. *Proc Indian Acad Sci. (Chem. Sci).*, 1995;107(2):123.
- Singh L, Mohan G, Parashar RK, Tripathi SP and Sharma RC. Studies on anti-inflammatory activity of some lanthanone complexes of bioactive organic molecules. *Curr Sci.* 1986;55: 846.
- Garg HJ and Prakash C. Potential antidiabetics VIII: 4-arylhydrazono-N'-guanylnitrate-3-methyl-2-pyrazolin-5-ones, 4-aryloxy-N'-guanylnitrate-3,5-dimethylpyrazoles, and 4-aryloxy-N'-guanylnitrate-3,5-diphenylpyrazoles, *J Pharm Sci.* 1971; 60:323.
- Cimerman Z, Miljanic S and Galic N. Schiff Bases Derived from Aminopyridines as Spectrofluorimetric Analytical Reagents, *Croatica Chemica Acta.* 2000;73(1):81- 95.
- Singh P, Goel R L and Singh B P. *J Indian Chem Soc.* 1975;52:958.
- Perry BF, Beezer AE, Miles RJ, Smith BW, Miller J and Nascimento MG. *Microbois.* 1988; 45:181.
- Elmali A, Kabak M and Elerman Y. *J Mol Struct.* 2000;477:151.
- Patel PR, Thaker BT and Zele S. *Indian J Chem.* 1999;38A:563.
- Zhen-Feng Chen, Yan-Cheng Liu, Li-Min Liu, Heng-Shan Wang, San-Hai Qin, Bo-Long Wang, He-Dong Bian, Bin Yang, Hoong-Kun Fun, Hua-Gang Liu, Hong Liang and Chris Orvig. Potential new inorganic antitumour agents from combining the anticancer traditional Chinese medicine (TCM) liriodenine with metal ions, and DNA binding studies, *Dalton Trans.* 2009;38(2):262-272.
- Zhen-Feng Chen, Li Mao, Li-Min Liu, Yan-Cheng Liu, Yan Peng, Xue Hong, Hong-Hong Wang, Hua-Gang Liu and Hong Liang. Potential new inorganic antitumour agents from combining the anticancer traditional Chinese medicine (TCM) matrine with Ga(III), Au(III), Sn(IV) ions, and DNA binding studies. *J Inorg Biochem.* 2011;105(2):171-180.
- Arai E, Nishida Y, Wasa J, Urakawa H and Zhuo L. Inhibition of hyaluronan retention by 4-methylumbelliferone suppresses osteosarcoma cells in vitro and lung metastasis in vivo *British Journal of Cancer.* 2011;105:1889-1849.



18. (a) John VD and Krishnankutty K. Antitumour activity of synthetic curcuminoid analogues (1,7-diaryl-1,6-heptadiene-3,5-diones) and their copper complexes, *Appl. Organometal. Chem.*, 2006;20:477.  
(b) John VD and K. Krishnankutty. *Transition Met Chem.* 2005;30:229.  
(c) V. John VD and K. Krishnankutty. *Synth React Inorg. Met.-Org Chem.* 2003;33(2):343.
19. John VD, Kuttan G and Krishnankutty K. *J Exp Clin Cancer Res.* 2002;21(2):219.
20. Khopde SM, Priyadarsini KP, Venketesan P and Rao MNA. Free radical scavenging ability and antioxidant efficiency of curcumin and its substituted analogue. *Biophys Chem.* 1999; 80:85.
21. Antony S, Kuttan R and Kuttan G. Immunomodulatory Activity of Curcumin, *Immun. Invesig.* 1999;28:291.
22. Anto RJ, Babu KND, Rajasekharan KN and Kuttan R. Anti-tumour and antioxidant activity of natural curcuminoids, *Cancer Lett.* 1995;94;79.
23. Vogel's text book of Practical Organic Chemistry, 5<sup>th</sup> Edition, ELBS. 1193.
24. (a) Duff JC and Bills EJ. *J Chem Soc.* 1932;1987. (b) Ferguson LN. The Synthesis of Aromatic Aldehydes. *Chem Rev.* 1946;38:227-254.
25. Bellamy LJ. *The Infrared Spectra of Complex Molecules*. 3<sup>rd</sup> Ed, Methuen, London.1966.
26. Yongxiang Ma, Zhengzhi Zeng, Yun Ma and Gang Zhao. Chelate complexes of formylferrocene m-nitrobenzoylhydrazone with lanthanide, *Inorg. Chim. Acta,* 1989;165:185.
27. Nakamoto K. *The Infrared Spectra of Inorganic and Coordination Compounds*, 2<sup>nd</sup> Ed, Wiley Interscience, New York, 1970.
28. Puri Sharma and Kalia. *Principles of Inorganic Chemistry.* Milestone Publications, New Delhi, 2008.
29. Robert Milton Silverstein, Francis X. Webster and David J. Kiemle *Spectrometric identification of organic compounds,* John Wiley & Sons, 2005;ISBN 0471393622.