Structural Characterization and Bio-Activity Study of Schiff Base Metal Complexes

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Abstract- **The structural modification of organic molecules has considerable biological relevance and co-ordination of these compounds to metal ions significantly alters their biological activity. With this views , some Schiff base ligands are synthesized by the condensation of unsub/sub. aminothiazole with salicyl/napthyl aldehyde and their metal complexes with trasition metals. Cu(II),Ni(II),Zn(II) and Co(II) are prepared by adopting earlier procedure1. The complexes are characterized by elemental analysis, spectral study as well as by magnetic moment measurement. The structural elucidation of the molecules is based on electronic, IR, NMR as well as Magnetic Susceptibility measurement. The data are indicative of the fact that metal is bonded to ligand through phenolic oxygen and imino nitrogen atom. The anti-microbial assay of the prepared samples are carried out by adopting modern protocol and found to be good antibacterial and antifungal agents2.**

Index Terms- **unsub/sub, thiazole, salicyl/napthyl aldehyde, transition metal complexes, Schiff base derivatives, spectral study, antimicrobial assay.**

INTRODUCTION

The discovery of novel active molecules against new target is a matter of urgency to overcome the alarming problem of microbial resistance to antibiotics. With the developing knowledge on properties of functional groups nature of the donor atoms, the central metal ion, ligand with imine/azomethine groups are used for complexion studies. Especially tetra dentate Schiff base with N2O2 donors are well known to co-ordinate with many metal ions and their complexes play an important role in biological, chemical and analytical fields1.It has been reported by many workers2 that Organic molecules complexes with metal ions exhibit better biological activity compared to compound alone, hence are used as effective drugs3-5.

Henery et. al4 have synthesized some Schiff bases and their transition metal complexes with Cu(II),Ni(II) & Zn(II) and reported their biological activity. Metal complexes of some Schiff base derivatives have been prepared by Nair et al.1 and their antimicrobial activity against some clinically important bacteria is reported1. Synthesis, characterization and fungicidal activity of some quinazalone derivative has been studied by pattanaik et al.2 and found to be good fungicidal agents.

The present work aims to prepare, characterize and study the antimicrobial and antifungal activities of some metal complexes derived from Schiff base ligands and transition metals by adopting modern techniques5-7.

EXPERIMENTAL

The chemicals used were of A.R grade and doubled distilled water was used throughout the experiment. Purity of the ligands as well the complexes was checked by TLC and HPLC study.

SYNTHESIS OF SCHIFF BASE LIGANDS

Mixture of derivatives of amino thiazole(1 mole) , Sub./Unsub, Salicyl/Napthyl aldehyde (1 mol) in ethanol(30-35mL) and piperidine (3-4 drops) was refluxed on a water bath for about 1hr.After completion of the reaction, the product was cooled, filtered and recrystallized from ethanol8.

SYNTHESIS OF METAL COMPLEXES

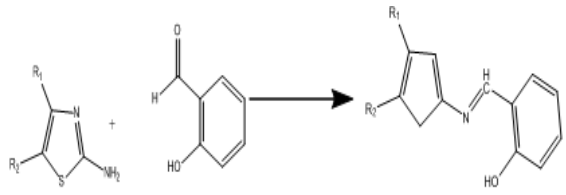
The prepared ligands in benzene was added to solution of different metal acetates(0.5 mol)in

methanol with stirring for 30-40 minutes and the solid thus separated was filtered , washed 2-3 times with hot methanol and benzene. Analytical data of the complexes and ligands are obtained by carrying out different studies.

SYNTHESIS ROUTES

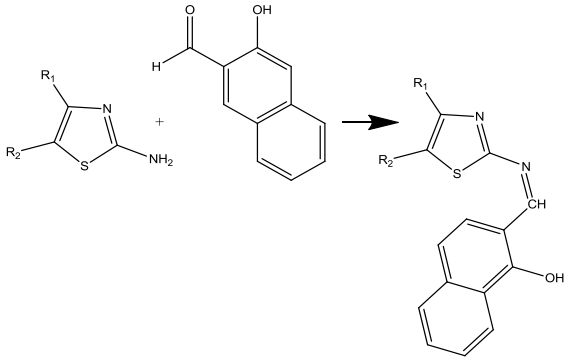
Preparation of Schiff base:

Route-1



2-imino-(o-hydroxyarylidine-4-sub.thiazole)

Route-2



2-imino-(o-hydroxynapthylidine-4-sub.thiazole)

PHYSICAL MEASUREMENT

Melting point of the complexes were determined and was uncorrected .Elemental analysis was carried out by Brooker, C.H.N & S analyzer.Electronic spectra was recorded in DMSO using Schimadzu UV-Visible(F.T.) 1601 Spectrophotometer.IR Spectra was determined by Perkin-Elmer 337 grating FTIR in KBr disc 1H NMR was taken in CDCl3 on a Bruker instrument using TMS as Internal Standard.Mass spectra of two of the prepared ligands ;when R→OH,OCH3 and their Co(II) & Zn(II) complexes were recorded at a voltage of 70 ev and the characteristic peaks with their intensities relative to base peak=100 was determined.

Magnetic Susceptibility of the metal complexes was measured by a Guoy Balance at room temperature , calibrating the Guoy tube with HgCo(SCN) complex and diamagnetic corrections were made employing the data of Lewis & Willkins.9

RESULT AND DISCUSSION

The complexes are fairly soluble in alcohol,spirangly soluble in acetone but insoluble in benzene and water.Many of them have not sharp M.P but decompose in the temperature range,180-3000C (Table1&2).The analytical data of the complexes satisfactorily agree with the M.F:ML2(L=Schiff base ligand anion)

Table-1(Physical data of complexes) Series-1

				%N		%M	
Sl. No	R_1	M	M.P(°C)	C	F	C	F
1	p-$OMeC_6H_4$	Ni	180	3.71	4.13	8.61	8.70
2	p-MeC_6H_4	Ni	185	4.02	4.30	8.89	9.14
3	p-ClC_6H_4	Ni	>300				
4	p-$OMeC_6H_4$	Zn	145	3.82	4.08	9.21	9.54
5	p-MeC_6H_4	Zn	290	4.01	4.30	9.75	9.98
6	p-ClC_6H_4	Zn	>300	3.81	4.05	9.97	9.19
7	p-$NO_2C_6H_4$	Zn	235	5.01	5.65	8.62	9.10
8	C_6H_5	Cu	212	4.21	4.40	9.97	10.10
9	p-$NO_2C_6H_4$	Cu	265	5.17	5.60	8.01	8.52
10	p-ClC_6H_4	Cu	>300	3.81	4.01	8.97	9.91
11	p-ClC_6H_4	Co	>290	7.11	7.19	7.62	7.90
12	p-MeC_6H_4	Co	188	7.5	7.10	8.05	8.24
13	p-$NO_2C_6H_4$	Co	230	6.93	7.17	7.42	7.85
14	p-$OMeC_6H_4$	Co	184	7.19	7.37	7.71	8.07
15	C_6H_5	Co	210	7.79	8.02	8.35	8.49

The % C & H found by analysis is varying within 5% from the theoretical value and the yield is within 60-70%

Table-2(Physical data of complexes) Series-2

				%N		%M	
Sl.No	R_1	M	M.P(°C)	F	C	F	C
1	ClC_6H_4	Cu	251	3.25	3.54	7.91	8.03
2	ClC_6H_4	Ni	235	3.21	3.58	6.91	7.50
3	ClC_6H_4	Zn	>280	3.22	3.53	8.02	8.20
4	ClC_6H_4	Co	>284	7.11	7.19	7.62	7.90
5	$CH_3C_6H_4$	Cu	>280	3.48	3.68	8.17	8.36
6	$CH_3C_6H_4$	Ni	255	3.33	3.75	8.01	7.92
7	$CH_3C_6H_4$	Zn	261	3.61	3.72	8.20	8.65
8	$CH_3C_6H_4$	Co	267	7.5	7.10	8.05	8.24
9	$O_2NC_6H_4$	Cu	255	4.69	5.17	7.43	7.82
10	$O_2NC_6H_4$	Ni	278	4.82	5.20	7.05	7.31
11	$O_2NC_6H_4$	Zn	258	4.88	5.16	7.89	7.99
12	$O_2NC_6H_4$	Co	264	6.93	7.17	7.42	7.85
13	C_6H_5	Cu	235	3.51	3.88	8.59	8.80
14	C_6H_5	Ni	222	3.71	3.90	8.10	8.23
15	C_6H_5	Zn	210	3.73	3.87	8.45	8.99
16	C_6H_5	Co	228	7.79	8.02	8.35	8.49

The % C & H found by analysis is varying within 5% from the theoretical value and the yield is within 60-70%

SPECTRAL DATA

The Electronic Spectra of free ligands show an intense band centred at 360 nm attributed to n-π* of the azomethine group(>N-CH-).Another band at higher energy region in case of Schiff base is due to π- π* transition of the benzene ring which are also found in case of complexes but are shifted to a lower frequencies confirming the co-ordination of the ligands to metal ions.

I.R.SPECTRA

I.R.Spectra of the ligand molecules exhibit a strong sharp band in the region ; 1630-1615 cm-1 corresponding to (>C=N)stretching bands at 1605,1530,1460 & 1430 cm-1 due to thiazole and phenyl ring vibrations but the metal complexes show bands at 1585-1580 cm-1(>C=N) without any change in other peaks.The shifting of the band from 1630-1615cm-1 to 1585-1580 cm-1 by complexation suggests the co-ordination in these compounds has taken placed through nitrogen atom of the azomethine group.The M-O bond formation is evidenced from shift of phenolic C-OH stretching band at 1280cm-1 in ligands to a higher frequency, 1330cm-1 in case of metal complexes .All these data suggest that the chelation of metal ion has taken place through N & O atoms of the ligands11.

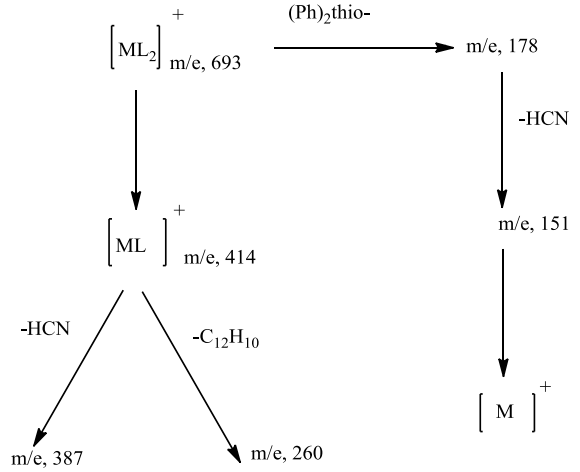
1H NMR

The 1H NMR spectra of the ligands in CDCl3 exhibit signals at 13.2, 6.4, 7.3 δ down field from TMS, which are assigned to enolic 'OH' and phenyl group protons respectively.But in case of complexes there is absence of signal corresponding to enolic 'OH' proton confirms it's de protonation and subsequent involvement in co-ordination.The chemical shift found for 'OH' proton in case of ligands (10.2 ppm, 10.7 ppm) is not found in any of the complexes , indicating the bonding of oxygen to metal ions(M-O-C)12.The 1H NMR data also in confirmation with I.R. Spectral value.

MASS SPECTRA

The mass spectra of the metal complexes exhibit stable molecular peaks and no peak with m/e ratio higher than the molecular ion peak , ML2+ is found ruling out the possibility of formation of any polymeric species. The primary fragmentation pattern of metal complexes of three chelates are identical as seen in case of bis-ω-2(4,5-diphenyl-thiazole)-salicylideno iminato Co(II).

FRAGMENTATION PATTERN

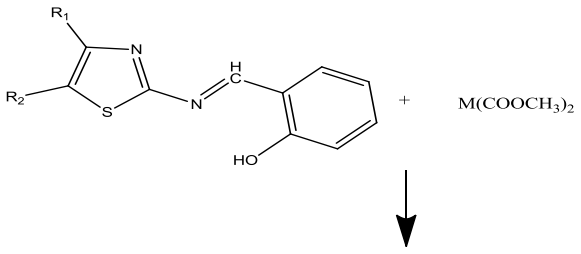


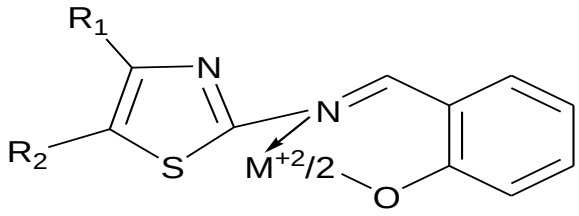
L = 2-(4,5- diphenyl thiazolyl)- unsub.- salicylidine iminato Co(II)

MAGNETIC MOMENT MEASUREMENT

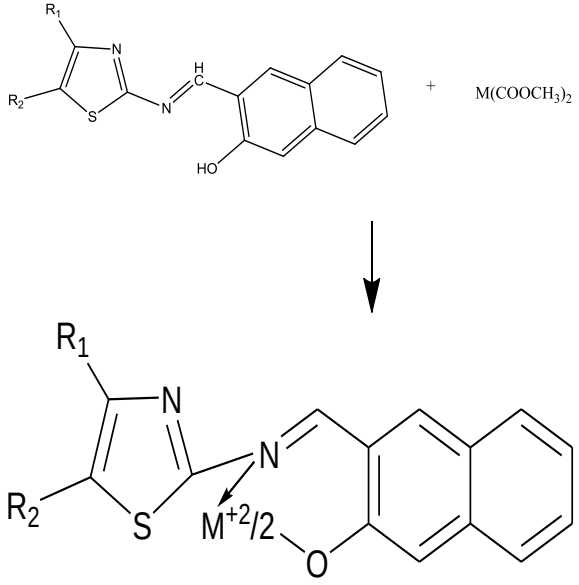
The magnetic moment of the complexes ; Co(II), Ni(II), Cu(II) & Zn(II) lies in the range 4.82-5.1, 3.0-3.2 B.M and 1.7- 2.0 BM respectively suggesting their octahedral nature13.

The magnetic moment of Co(II) complexes lies in the range 4.8- 5.1BM suggesting high spin octahedral compounds (A multiple band in the region , 18000-23000cm-1) also supports the above structure of the Co(II) complexes instead of tetrahedral or square planar as suggested by their empirical formula.The complexes of Ni(II) & Cu(II) show magnetic moment at 3.0 – 3.2 BM and 1.7 – 2.0 BM suggesting the octahedral structure of the complexes13,14,15,16 on the basis of analytical and spectral data the following structures are assigned to the prepared complexes.





Series-I



Series-II

BIOLOGICAL ACTIVITIES

Anti-microbial Activity:

The prepared complexes are separated for their Anti-bacterial potency against the species: A pyrozonus, E.Coli, staphylocus Aurus by agar-plate method.Chloro-amphinicol is used as standard drug at a concentration of 10mg/mL. The result is compared with the free ligands and their metal complexes .It is evidenced from the data that:

[1] The free ligand and the metal complexes show +ve effect towards staphylococcus aurus more than standard.

[2] The biological activity of Ni(II) complex is higher than that of others.

[3] The free ligand as well as complexes exhibit higher antibacterial activity compared to standard.

[4] But Zn(II) complex show more activity compared to others.

The increased activity of metal chelates is explained on the basis of chelation theory.17 On chelation the polarity of metal ion is reduced to greater extent due to overlap of ligand orbitals and partial sharing of it's positive charge with donor groups.18 There is also increase in delocalisation of π electrons over the whole chelating ring , thus enhancing the penetration of the complexes into lipid membranes and blocking the metal binding sites in the enzymes of micro-organisms.19 These complexes also disturb the respiration process of the cell, blocking the synthesis of proteins which restricts the further growth of the organisms.20

The antifungal activity:

The antifungal potency of the ligands as well as complexes were evaluated by poisoned food technique using cuvular species21 and the % of inhibition was calculated as

% inhibition=(1- X/Y) x 100

X→ Growth of fungus with the complex

Y→ Growth of fungus in control

The fungicidal data are incorporated in tables 3A & 3B.

Some of the prepared complexes were screened for their anti-fungal activity22 on the fungus "Curvularia Species" and "selerotium rolfsii sace" by adopting poisoned food technique.The test was undertaken at three different concentrations and found to be active(100%) at highest one i.e. 200 ppm.

Table-3: Antifungal Activity of different complexes on Curvularia Species at 500 ppm

Sl.No	R_1	M	% of Inhibition at 500ppm on Curvularia Species 3(A)	% of Inhibition at 500ppm on selerotium rolfsii sace 3(B)
1	p-Cl	Cu	81.5	89.20
2	do	Ni	83.7	87.30
3	do	Zn	86.4	88.5
4	do	Co	83.9	86.8
5	p-NO2	Cu	82.1	87.4
6	do	Ni	81.05	86.20
7	do	Zn	80.2	82.30
8	do	Co	80.5	81.5
9	p-oMe	Cu	83.1	88.2
10	do	Ni	85.2	86.7
11	do	Zn	84.7	85.4
12	do	Co	83.5	86.0
13	p-Me	Cu	83.7	95.5
14	do	Ni	84.3	87.9
15	do	Zn	83.4	87.7
16	do	Co	82.7	86.8
17		Cu	81.5	84.25
18	do	Ni	82.2	83.1
19	do	Zn	82.7	82.7
20	do	Co	81.01	83.0

Table -4 (Fungicidal Activity on selerotium rolfsii sace at different concentions)

Sl.No	M	R_1	% of Inhibition		
			50ppm	100ppm	200ppm
1	Ni	$(OCH_3)C_6H_4$	60.22	76.7	100
2	Zn	$(OCH_3)_3C_6H_2$	75.37	88.06	100
3	Zn	$NO_2C_6H_4$	68.56	85	100
4	Zn	C_6H_5	66.66	89.39	100
5	Zn	ClC_6H_4	70.02	82.67	100
6	Zn	C_6H_5	64.01	76.78	100
7	Zn	$NO_2C_6H_4$	67.23	88.08	100
8	Zn	$(OCH_3)_3C_6H_2$	63.5	76.2	100

SEM (CXF) = 0.0065 SEM (Fungicide) =0.0026
CDII (CXF) =0.018
CD (ST) II=0.0073 SEM (Conc) II=0.002
SEM (Conc) II=0.0073
CD (Conc) II=0.006

CONCLUSION

The present study indicates that metal complexes exhibit better pharmaceutical properties in comparison to their corresponding Schiff bases. Though the antifungal, anti-bacterial, anti-tumor activities of the complexes are reported by many workers, the complex under present study has not got much attention. Hence some new metal complexes are synthesized by adapting some modified route and their anti-microbial, anti-fungal activity has been reported.

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