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Cu (II) METAL COMPLEXES OF SCHIFF BASES, PREPARATION, CHARACTERISATION AND BIOLOGICAL ACTIVITY

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Keywords:

Schiff bases, Cu (II) metal Complexes, Spectral analysis, Antimicrobial activity.

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ABSTRACT: Heterocyclic schiff bases of 2-amino-4, 6-dimethyl benzothiazole with selected heterocyclic α- hydroxy aldehyde and α-hydroxy ketones and their Cu (II) metal complexes have been synthesised. The Cu (II) metal complexes of schiff bases are reported and characterised based on elemental analysis, IR, ^{1}H NMR, ESR, XRD, Thermal analysis, magnetic moment, and molar conductance. The molar conductance data reveals that all metal chelates of schiff bases are non electrolytes. IR spectra show that ligand is coordinated to the metal ion in a bidentate manner. From the magnetic and electronic spectral data it is found that the geometrical structures of these complexes are square planar. The activity data show the metal complexes to be more potent antifungal and antibacterial than the parent schiff base ligands against one or more fungal and bacterial species.

INTRODUCTION: Schiff bases and their complexes have a variety of applications in biological, clinical, analytical and pharmacological areas. Studies of a new kind of chemotherapeutic Schiff bases are now attracting the attention of biochemists[1]. Earlier work reported that some drugs showed increased activity, when administered as metal complexes rather than as organic compounds. A large number of Schiff bases and their complexes have been studied for their interesting and important properties, e.g., their ability to reversibly bind oxygen, catalytic activity in hydrogenation of olefins and transfer of an amino group, photochromic properties, and complexing ability towards some toxic metals.

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The high affinity for the chelation of the Schiff bases towards the transition metal ions is utilized in preparing their solid complexes and the complexes are used as antitumor and antibacterial agents [2, 3]. A number of studies have reported the ligational aspects and biological role of Schiff bases and their metal complexes [4, 5]. Schiff bases are the condensation products of amines with active carbonyl compounds. They contain azomethine (> C = N-) group and act as effective ligands. The Schiff bases are generally represented by R – CH = N – R_1 and can be prepared by condensation of active carbonyl compound with primary amine.

EXPERIMENTAL

MATERIAL AND METHOD:

All the melting points were determined in an open capillary tube and are uncorrected. Completion of the reaction was monitored by thin layer chromatography on precoated sheets of silica gel G. All the reagents used were chemically pure and are of AR grade. The ligand selected in the preparation

of metal complexes are (4, 6-Dimethyl-benzothiazol – 2 - yl) - (1H-pyrrol-2-ylmethylene)-amine (L_1), (4, 6-Dimethyl-benzothiazol-2-yl)-pyridin-2-ylmethylene-amine (L_2) 4,6-Dimethyl-benzothiazol-2-yl) - pyridin - 2 – ylmethylene - amine (L_3), 1 - [(4, 6 - Dimethyl-benzothiazol – 2 - ylimino)- methyl] – naphthalene – 2 - ol (L_4), 2-[1-(4,7-Dimethyl-benzothiazol -2-ylimino)-ethyl]-benzene-1,4-diol (L_5). Transition metal Cu (II) was used for the synthesis of metal complexes with corresponding Schiff base ligand.

Synthesis of 2 – Amino - 4, 6 Dimethyl benzothiazole:

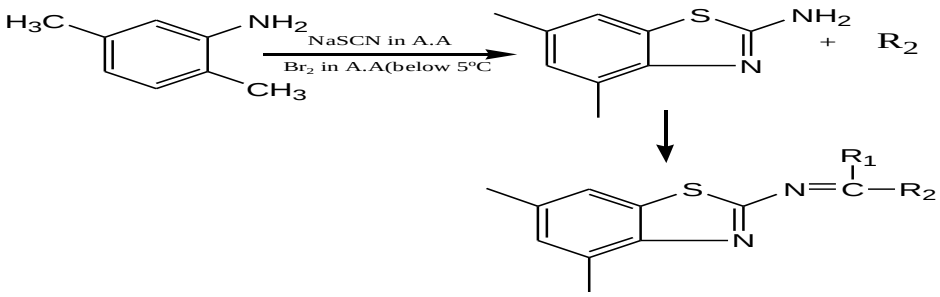
Synthesis of 2-amino-4, 6-Dimethyl Benzothiazole was carried out by the standard method.(0.1M) 2,4-Xylidine (2,4-dimethylaniline) and sodium thiocyanate (0.2M) in 100ml glacial acetic acid were mixed together and reaction mixture was cooled to 0^{o}C temperature.

(0.2M) bromine in acetic acid (25ml) was added to the above solution drop wise and the mixture was stirred till the complete addition of bromine maintaining temperature below 5°C throughout addition. Stirring was kept continued maintaining temperature below 5°C for half an hour after addition of Bromine is made. The solid thus obtained after complete addition of bromine was filtered on vacuum and then dissolved in hot water.

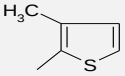
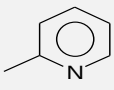
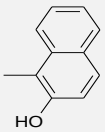
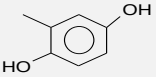
The solution was then treated with very dilute alkali like NaOH for the separation of free amine. The free amine thus obtained was filtered, washed and dried and was recrystallized from ethanol M.P observed 140°C, yield 80%. It was tested for free NH_2 group.

Synthesis of Schiff bases:

Schiff bases were synthesized by using equimolar ethanolic solutions of heterocyclic amine and hydroxyaldehyde / ketone and refluxing mixture for 4-5 hours. Then the reaction was monitored by TLC method. Upon observing single spot the heating was stopped and reaction mixture was poured in ice cold water / on crushed ice the separated solid was collected by filtration, after washing and drying, it was recrystallized from ethanol. The melting points were recorded.



SCHEME-I

Sr.No.	Compound	Substituents	
		R_1	R_2
1	L_1	H	
2	L_2	H	
3	L_3	H	
4	L_4	H	
5	L_5	CH_3	

Preparation of complexes: The ligand (0.02 moles) and the metal salt (0.01 moles) in 50 ml ethanol were mixed. The pH of the mixture solution was raised up to 5 using alcoholic ammonia .The solution was then concentrated on steam bath in a china bowl. Solid complex there after separate out washed with acetone to remove excess of ligand and dried over $CaCl_2$ overnight.

TABLE 1: ANALYTICAL DATA OF CU (II) COMPLEXES

Sr No	Molecular Formula	Mol. Wt.	Colour	M.P. ^oC	Elemental Analysis (%)				Mol. Cond. mhos cm^2 Mol^{-1}	μ eff. B. M.
					C (Cal) found	H (Cal) found	N (Cal) found	Metal (Cal) found		
1.	$Cu(C_{14}H_{12}SN_3)_2$	571	Heena	190	(58.64) 57.78	(4.20) 3.46	(14.71) 15.06	(11.03) 11.97	128	1.76
2.	$Cu(C_{15}H_{14}S_2N_2)_2$	635	Brown	>280	(56.69) 57.01	(4.40) 3.56	(8.81) 8.12	(9.92) 8.15	124	1.78
3.	$Cu(C_{15}H_{13}SN_3)_2$	597	Parrot Green	274	(60.30) 59.16	(4.35) 4.56	(14.07) 13.24	(10.63) 9.47	130	1.81
4.	$Cu(C_{20}H_{15}SN_2O)_2$	725	Faint Yellow	>280	(66.20) 65.37	(4.13) 3.69	(7.72) 6.22	(8.75) 8.86	121	1.84
5.	$Cu(C_{17}H_{15}SN_2O_2)_2$	685	Grey	>280	(59.52) 58.14	(4.36) 3.24	(8.15) 7.71	(9.32) 9.87	128	1.74

RESULT AND DISCUSSION:

Magnetic moment:

Magnetic susceptibility of Cu (II) complexes at room temperature exhibit magnetic moment in the range 1.75-1.84 B.M[6] which is characteristic of spin values for Cu (II) complexes. The values of the magnetic moment suggest the paramagnetic nature with one unpaired electron of all Cu (II) complexes indicating Square Planar geometry which is supported by the ESR spectral results. The magnetic moment values are given in Table

Electronic Spectral data:

For Cu (II) complexes Cu $(L_1)_2$ to Cu $(L_5)_2$ the electronic spectra showed bands in the range 22200 cm^{-1} to 41700 cm^{-1}i.e these spectral bands are observed near and above 3500cm^{-1} can be assigned to charge transfer transitions. The bands at 34400 cm^{-1} to 37037 cm^{-1} are typically characteristic for square-planar geometry for Cu (II) complexes[7]

TABLE 2: ELECTRONIC SPECTRAL DATA OF CU (II) COMPLEXES

Complexes code	$\mu_2 cm^{-1}$	$\mu_3 cm^{-1}$	LFSE(Kcal/mole)
Cu-L_1	37735	44052	107.5
Cu-L_2	26315	42372	74.99
Cu-L_3	37593	43668	107.1
Cu-L_4	25906	42735	73.83
Cu-L_5	29411	38910	83.82

IR Spectra:

In the IR spectra of all Cu(II) complexes, medium to strong intensity bands appeared in the region 1627- 1637 cm^{-1}[8] which can be assigned to characteristic azomethine group i.e –(C=N) of almost all metal complexes. It is strikingly observed for all the metal complexes compared with ligands that the band value for azomethine group has shown considerable shifting in downward or upward depending upon the intensity of coordination which indicates the involvement of azomethine nitrogen in the coordination with metal ions[9].

The band value at ~1550 cm^{-1} shows no shift indicates non involvement of ring nitrogen in bonding. It is found that the band value absorbance in metal complexes is unchanged which strongly supports the non-involvement of thiazole nitrogen in coordination with metal ion. Further the band observed at ~3450cm^{-1} in ligand L_4 and L_5 is attributed due the presence of -OH. Either it is disappeared on complexation or showed variance in frequency in downward direction which indicated the deprotonation and involvement in the coordination with transition metal ions under investigation[10].

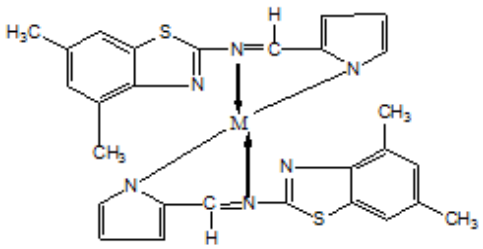
The bands at 825-840 cm^{-1} and 740-756 cm^{-1} in almost all metal complexes can be assigned due to C-S-C thiazole vibrations[11]. The appearance of non-ligand band at 555-600 cm^{-1} can be attributed to M-N band whereas the non-ligand band at 462-491cm^{-1} can be attributed to M-O band[12].

The appearance of these new bands of M-N and M-O vibrations supports the involvement of N and O atoms in complexation with metal ions. The IR spectra of Cu (II) complexes show band of medium

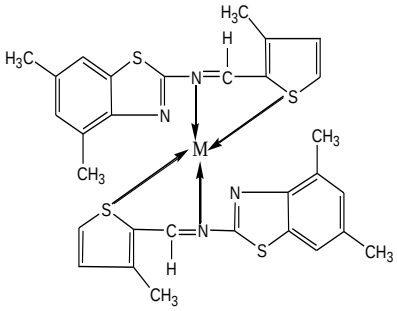
intensity at 3350-3500 cm^{-1} which can be assigned to –OH stretching due to presence of water of hydration, presence of water of hydration in these complexes is well supported and confirmed by the thermal data analysis and their respective spectral figures.

^{1}H-NMR Spectra:

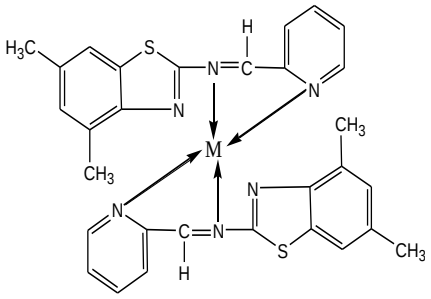
^{1}H NMR spectra of synthesized metal complexeswere recorded in DMSO. The ^{1}H NMR spectra of complexes show broad signals due to presence of metal ion and the conformation of each signal in the aromatic region is difficult due to complex pattern of splitting.



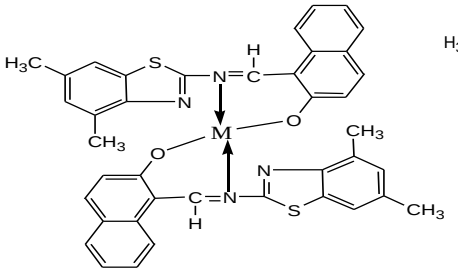
M= Cu(II) complex of ligand L_1



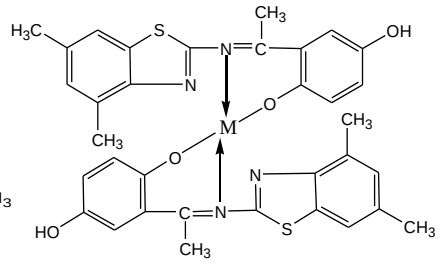
M= Cu(II) complex of ligand L_2



M= Cu(II) complex of ligand L_3



M= Cu(II) complex of ligand L_4



M= Cu(II) complex of ligand L_5

ESR Spectra: It is observed from ESR spectrum Cu (II) complexes that there is a single line resulting in the interaction of unpaired electron present in Cu (II) nucleus. The Table reveals that the 'g_{av}' values less than 2.3 which suggest the existence of sufficient covalent nature of metal ligand bond[13]. Also the G values less than 4 indicate that the Cu (II) complexes are strong field ligands. [Cu $(L_1)_2$] complex shows isotropy as the values of g|| and g⊥ are same were as rest of the three complexes show anisotropy. The electronic spectral data suggest that all Cu (II) complexes of ligands under study have square-planar geometry.

TABLE 3: ESR SPECTRAL VALUES OF Cu (II) COMPLEXES

Complex code	g_{II}	$g_{\wedge}$	g_{av}	G Axial symmetry parameter	μ_{eff} BM from Gouy Balance
$Cu(L_1)_2$	1.857	1.857	1.857	1	1.73
$Cu(L_3)_2$	1.870	1.821	1.837	0.72	1.74
$Cu(L_4)_2$	1.869	1.881	1.861	0.91	1.76
$Cu(L_5)_2$	1.552	1.652	1.618	1.28	1.72

X-Ray Diffractogram: X-ray diffractograms of the metal complexes under investigation show good intense peaks indicating high crystallinity Lattice parameter values as a = b ≠ c and α = β = γ which suggest Tetragonal Crystal Structure of P type lattice for Copper complex of Ligand L_4. Lattice parameter values as a ≠ b ≠ c and α = γ ≠ β which suggest Monoclinic Crystal Structure of P type lattice for Copper complex of Ligand L_1, L_3. Lattice parameter values as a = b ≠ c and α = γ ≠ β which suggest Hexagonal Crystal Structure of P type lattice for Copper complex of Ligand L_5.

ANTIMICROBIAL ACTIVITY

Antibacterial Activity:

The antibacterial activity was measured by agar cup method. Nutrient agar (Himedia) was prepared and sterilized at 15 Psi for 15 minutes in the autoclave. It was allowed to cool below 45 °C and seeded with turbid suspension of test bacteria separately, prepared from 24 hours old slant cultures. 3% inocula were used every time. The bacterial cultures selected were, two gram negative cultures viz. *Escherichia coli, salmonella typhi* and two Gram positive cultures Viz. *Staphylococcus aureus, Bacillus subtilis*.

This seeded preparation was then poured in sterile petri plate under aseptic condition and allowed it to solidify Cups of 10 mm diameter were borered in the agar plate with sterile cork borer. 100 µl of compound solution prepared in the cup under aspectic condition with the help of micropipette. 100µl of DMSO was also placed in one of the cup as blank (negative control). A standard antibiotic disk impregnated with 10 units of penicillin was also placed on the seeded nutrient agar surface as standard reference antibiotic (positive control).

The plates were kept in refrigerator for 15 minutes to allow diffusion of the compound from agar cup into the medium. Then the plates were shifted to incubator at 37 °C and incubated for 24 hours. After incubation plates were observed for the zone of inhibition of bacterial growth around the agar cup. Results were recorded by measuring the zone of inhibition in millimeter (mm) using zone reader. Antibacterial Activity of the synthesized metal complexes are given in table.

Antifungal Activity:

Antifungal activity was performed by poison plate method. The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aspetic condition so as to get final concentration as 1%. Gresiofulvin was prepared as standard reference plate (positive control) *Aspergilus niger, penicillium chrysogenum, Fusarium moneliforme, Aspergillus flavu*s were selected as test fungal cultures.

They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5ml of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nicrome wire loop to form suspension.

The fungal suspension was spot inoculated on the plate's prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hours. After incubation plates were observed for the growth of inoculated fungi. Results were recorded as growth of fungi (no antifungal activity) reduced growth of fungi (moderate antifungal activity) and no growth of inoculated fungi (antifungal activity).
Antifungal Activity of the metal complexes are given in table

TABLE 4: ANTIMICROBIAL DATA OF Cu (II) COMPLEXES

		Bacterial Strain				Fungal Strain			
Sr.No	**Comp.**	**Ec**	**St**	**Sa**	**Bs**	**An**	**Pc**	**Fm**	**Af**
1	Cu - L_1	22	21	25	26	-ve	-ve	-ve	-ve
2	Cu - L_2	11	16	23	28	-ve	-ve	-ve	-ve
3	Cu - L_3	28	24	31	37	-ve	-ve	-ve	-ve
4	Cu - L_4	19	21	32	35	-ve	-ve	-ve	-ve
5	Cu - L_5	20	25	28	35	-ve	-ve	-ve	-ve
6	DMSO	-ve	-ve	-ve	-ve	NA	NA	NA	NA
7	Penicillin	13	18	36	18	NA	NA	NA	NA
8	+ve control (blank)	NA	NA	NA	NA	+ve	+ve	+ve	+ve
9	(Grysofulvin)	NA	NA	NA	NA	-ve	-ve	-ve	-ve

Ec-E.coli, St-S.typhi, Sa- S.aureus, Bs-B.subtilis; An-A.niger, Pc-P.chrysogenum, Fm-F.moneliformae, Af-Aspergillus flavus; -ve: No growth of fungi,+ve; Growth of fungi, RG-Reduced growth, NA-Not Applicable, Zone of inhibition was measured in mm.

CONCLUSIONS: In summary, we have synthesized some Cu (II) complexes of Schiff bases. All the synthesized metal complexes gave satisfactory spectral and analytical data. The screening of antimicrobial data revealed that the all complexes show good antimicrobial activity.

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