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Synthesis, Evaluation of Structure & Biological Activity of Transition Metal Complexes of Sulpha Drugs

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ABSTRACT

Some new transition metal complexes of Cu (II), Zn (II), Mn (II) and Cr (III) are derived from Sulpha drug. Their structure has been characterized on the basis of elemental analysis, IR and ^{1}HNMR spectroscopy. The isolated products are coloured solids, soluble in DMSO, DMF and MeOH. The spectral data suggests that Schiff base acts as bidentate ligand and an octahedral environment exist around the metal ion. In search for better fungicides and bactericides, biocidal studies were conducted against the organisms *Escherichia coli, Salmonella typhi, Bacillus subtilis, Staphylococcus aureus, Aspergillus flavous, Aspergillus niger, Penicillium citrinum and Fusarium oxysporum.* The results suggests that the metal complexes of Schiff base proved to be excellent bactericides and fungicides in the present investigations.

KEYWORDS: Cu (II), Zn (II), Mn (II) and Cr (III) complexes, IR and ^{1}HNMR spectroscopy and biological activity.

INTRODUCTION

Sulpha drugs are a group of compounds which show a large spectrum of biological activities.[1] The Schiff bases and the metal complexes derived from sulpha drugs are used for eliminating a wide range of infections in human and other animal systems. These compounds are observed to be effective antifouling,[2] antibacterial[3], antiviral, antitumour[4] and anti oncogenesis[5] agents, they are also used commercially as bactericides[9], fungicides[6], ascaricides[7], and industrial and agricultural biocides[8]. The pronounced biological activity of the transition metal complexes of Schiff bases derived from sulpha drugs has led to considerable interest in their coordination chemistry. The condensation products of sulpha drugs with aldehydes are biologically active Schiff bases which have good complexing ability; their activity increases on complexation with transition metal ions. Keeping this in view, it was considered worthwhile to synthesize transition metal complexes of Schiff bases derived from sulpha drugs.

EXPERIMENTAL

All the chemicals used were of AR grade. The liquid reagents were purified by distillation.

p-Furfurylidene aminobenzene sulphonamide (SF) was synthesized by refluxing on water bath, a mixture of 7.6g Sulpha drug and 3.8ml of Furfuraldehyde in 60ml Ethanol for two hours. On cooling the Schiff base (SF) separated out as white shining crystals. It was filtered washed, dried and finally recrystallised from hot ethanol solution.

The Cu (II), Zn (II), Mn (II) and Cr (III) complexes of Schiff base were prepared by refluxing on water bath, a mixture of 0.01 mole of metal chloride (i.e 1.70g of $CuCl_2$. $2H_2O$, 1.36g of $ZnCh_2$, 1.97g of $MnCl_2$. $4H_2O$, and 2.66g of $CrCl_3$. $6H_2O$) in 15ml ethanol respectively with 0.02 mole of Schiff base SB (i.e5.8g of SB) in 20ml ethanol for three hours. The reaction mixture was concentrated and then cooled. The solid derivatives were separated out. These were filtered, washed and finally air-dried.

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For the microanalysis of C,H and N, CHN Perkin-Elmer micro analyzer-240 was used. The metal contents of the complexes were analyzed by standard methods. The IR spectra of the Schiff base and its metal complexes were recorded on Perkin-Elmer 4250 spectrophotometer in the range 4000-200 cm-[1] in CSI/KBr matrix. The [1]HNMR spectra of the Schiff base and the metal complexes were recorded in $CDCl_3$ on a Bruker DRX 300F, 300 MHz FTNMR spectrometer.

RESULT AND DISCUSSION

The obtained metal complexes of the Schiff base (SF) are coloured solid, insoluble in water but soluble in benzene, acetone, DMF and other polar organic solvents. Elemental analyses suggests 1:2 (M:L) stoichiometry.[9] All the physical and analytical results are listed in Table-1.

Table-1:Physical & Analytical Data of Schiff base (SF) and its metal complexes

COMPOUND	MOL. WT.	COLOUR	M.P. (ºC)	ELEMENTAL ANALYSIS % FOUND (CALCULATED)				
				C	H	N	S	METAL
SF [$C_{11}H_{10}O_3N_2S$]	250	YELLOW	180º-182º	52.44 (52.80)	3.37 (4.0)	11.33 (11.20)	12.67 (12.80)	- -
Cu-SF [$Cu(C_{22}H_{20}N_4O_6S_2).2H_2O$]	599	DARK BROWN	146ºC	44.12 (44.07)	4.17 (4.01)	9.02 (9.34)	10.54 (10.68)	10.33 (10.51)
Zn-SF [$Zn(C_{22}H_{20}N_4O_6S_2).2H_2O$]	601	LIGHT YELLOW	155ºC	43.83 (43.92)	3.84 (3.99)	9.33 (9.31)	10.55 (10.64)	10.94 (10.81)
Mn-SF [$Mn(C_{22}H_{20}N_4O_6S_2).2H_2O$]	591	LIGHT BROWN	173ºC	44.64 (44.67)	4.01 (4.06)	9.66 (9.47)	10.75 (10.82)	9.94 (9.30)
Cr-SF [$Cr(C_{22}H_{20}N_4O_6S_2).2H_2O$]	588	DARK GREEN	180ºC	44.75 (44.90)	4.17 (4.08)	9.64 (9.52)	10.93 (10.88)	8.96 (8.84)

Infra Red Spectra

The IR Spectra[10] of the Schiff base and the metal complexes show sharp bands in the region 3200-3300 cm^{-1} and 1570-1590 cm^{-1} attributed to the stretching and bending vibrations respectively of ν (NH_2). While the symmetric and asymmetric vibrations of ν (SO_2) are observed in the region 1150-1160 cm^{-1} and 1310-1330 cm^{-1} respectively. The IR Spectra of Schiff base show a sharp band at 1611 cm^{-1}, attributed to ν (C=N) azomethine linkage[11] a shift of ±15 cm^{-1} is observed in this frequency in case of metal complexes which is suggestive of the coordination of the metal ion with the azomethine linkage. The band in the far IR spectra of metal complexes in the region 550-560 cm^{-1} are tentatively assigned to ν (M—N) vibrations. The stretching and bending vibrations found in the region 670-690 cm^{-1} and 830-850 cm^{-1} respectively are attributed to the coordination of water molecules. The I R spectral data in reported in Table-2

Table-2:Tentative assignments of some selected bands in the IR spectra (cm^{-1}) of Schiff base (SF) and its metal complexes

Compounds	ν(NH_2) (strech.)	ν(NH_2) (bend.)	ν(SO_2) (sym.)	ν(SO_2) (asym)	ν(C=N)	ν(H_2O) (stretch.)	ν(H_2O) (bend.)	ν(M-N)
SF	3289	1582	1153	1329	1626	-	-	-
Cu-SF	3322	1547	1152	1329	1620	690	851	515
Zn-SF	3290	1582	1153	1327	1616	679	842	551
Mn-SF	3290	1582	1153	1329	1608	678	842	559
Cr-SF	3294	1583	1153	1328	1611	671	843	552

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^{1}HNMR Spectra:

The ^{1}HNMR spectra of the Schiff base and its metal complexes show multiplet signals in the region δ 6.67-8.40 ppm due to the benzene ring protons, while the signals due to HC=N protons[12] appear at δ 4.73 ppm in the spectra of Schiff base while it shifts downfield in the spectra of corresponding metal complexes. The broad signals due to $–NH_2$ protons also shift downfield in the spectra of metal complexes. Thus, this downfield shift is attributed to the complex formation i.e. attachment of metal with nitrogen atom of $–NH_2$ group and nitrogen atom[13,14] of HC=N group. The evidences mentioned above supports the complexes formation of the Schiff base. The ^{1}HNMR data is given in Table-3

Table-3:^{1}HNMR Spectral data of Schiff base (SF) and its metal complexes

S.No.	Compound	Chemical Shift, δ.(ppm)	Peak position	Group Assigned.
1.	SF	(a) 6.61-8.28 (b) 4.67 (c) 10.00 (d) 6.10	Multiplet Singlet Singlet Singlet	Aromatic ring HC=N $-NH_2$ Furan ring
2.	Cu-SF	(a) 6.76-8.31 (b) 4.81 (c) 10.12 (d) 6.11	Multiplet Singlet Singlet Singlet	Aromatic ring HC=N $-NH_2$ Furan ring
3.	Zn-SF	(a) 6.66-8.32 (b) 4.78 (c) 10.17 (d) 6.10	Multiplet Singlet Singlet Singlet	Aromatic ring HC=N $-NH_2$ Furan ring
4.	Mn-SF	(a) 6.74-8.29 (b) 4.89 (c) 10.21 (d) 6.12	Multiplet Singlet Singlet Singlet	Aromatic ring HC=N $-NH_2$ Furan ring
5.	Cr-SF	(a) 6.63-8.29 (b) 4.96 (c) 10.16 (d) 6.10	Multiplet Singlet Singlet Singlet	Aromatic ring HC=N $-NH_2$ Furan ring

Structure of the Complexes:

On the basis spectral data the following tentative structure of metal complexes of Schiff base (SF) have been proposed:

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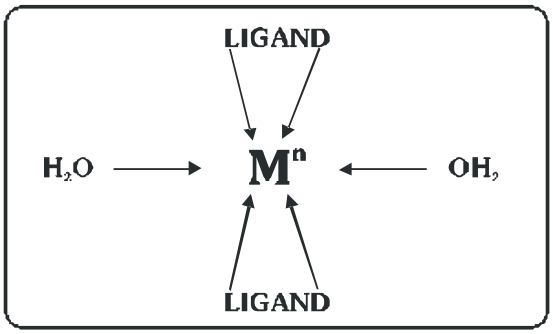

Fig 1: Tentative structure of the metal complexes

Where M^n = Cu (II), Zn (II), Mn (II) and Cr (III) metal ions

BIOLOGICAL ACTIVITY:

Antibacterial Activity:

The bactericidal activity was evaluated by the filter paper disc diffusion method. The nutrient agar medium (Peptone, beef extract, NaCl and agar-agar) and 5mn diameter paper disc of Whatman N0.1 were used. The compounds sere dissolved in DMF in 100, 250 and 500 ppm concentrations. The filter paper discs were soaked in different solutions of the petridishes already seeded with the test organisms. The plates were incubated for 24 hours at 37ºC and the inhibition zone around each disc was measured.

Antifungal Activity:

The fungicidal activity was evaluated by Agar plate technique. The fungi were grown in agar medium (glucose 20g, starch 20g, agar-agar 20g and 1000ml water) at 28±2ºC and the compounds after being dissolved in DMF were mixed in the medium. The growth of the fungus was obtained by measuring the diameter of colony in petridishes after 3days and the percentage inhibition was calculated by the formula:

$$\%\ inhibition\ = \frac{(C-T)\ \times\ 100}{C}$$

Where C and T are the diameters of the fungus colony in control and test plates respectively.

Antibacterial and Antifungal Activities:

The Schiff base (SF) as well as the metal complexes exhibited good amount of activity against all the tested bacterial and fungi as reported in Table-4 and Table-5 respectively.The Schiff base along with its metal complexes showed maximum activity against the bacteria, E. coli and minimum against the bacteria, *S. aureus* though, the fungicidal studies reveal that the activity was maximum against *A. niger* followed by *F. oxysporum*, *A. flavous* and *P. citrimum.*

The metal complexes were found to be more toxic as compared to their parent Schiff base.[15] In general the activity of the metal complexes was in the following order:-

Cr (III) > Mn (II)> Zn (II)> Cu (II)

The increased activity of metal complexes may be due to the effect of the metal ion configuration and the charge on normal cell. A possible mode of toxicity may be specified by Chelation Theory.[16] Chelation considerably reduces the polarity of the metal ion mainly because of partial sharing of its π-electrons and delocalization over the whole chelate ring.[17] Such chelation increases the lipophilic character of metal chelate, which probably tends to breakdown the permeability barriers of cells, resulting in the interference with the normal cell process.[18] thus the results suggests that the metal complexes of Schiff base (SF) proved to be excellent bactericides and fungicides in the present investigations.

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Table-4:**Antibacterial activity of Schiff base (SF) and its metal complexes**

Compound	Conc. In ppm	Zone of Inhibition (in mm)			
		E. Coli	*S. typhi*	*B. subilis*	*S. aureus*
SF	500	38	35	34	23
	250	25	23	25	20
	100	15	10	15	-
Cu-SF	500	45	42	40	32
	250	30	30	32	25
	100	17	15	16	-
Zn-SF	500	48	45	45	35
	250	35	30	32	25
	100	17	16	18	-
Mn-SF	500	50	50	48	38
	250	35	32	35	27
	100	20	18	18	12
Cr-SF	500	54	52	50	46
	250	42	36	38	32
	100	25	22	22	18

Table-5: Antifungal activity of Schiff base (SF) and its metal complexes.

Compound	Conc. In ppm	Average percentage Inhibition			
		A. flavous	A. niger	P. citrinum	F. oxysporum
SF	500	31.37	23.21	26.92	24.07
	250	21.56	19.64	17.30	18.51
	100	9.80	14.28	9.61	14.81
Cu-SF	500	68.62	71.42	71.15	68.51
	250	62.74	62.50	57.69	61.11
	100	29.41	41.07	40.38	40.74
Zn-SF	500	74.50	87.50	73.07	83.33
	250	62.74	55.35	59.61	72.22
	100	41.17	44.64	34.61	42.59
Mn-SF	500	78.43	82.14	80.76	83.33
	250	64.70	73.21	65.38	72.22
	100	33.33	50.00	34.61	40.74
Cr-SF	500	86.27	91.07	86.53	88.88
	250	68.62	57.14	69.23	72.22
	100	39.21	44.64	57.69	44.44

REFERENCES

1. S. Shah, R. Vyas and R. H. Mehta, J. Ind. Chem. Soc., 1992, 69, 590.
2. H.C. Rani, J. Indian Council Chem., 2005, 22 (2), 15.
3. S.N. Pandeya, D. Sriram and G. Nath, Eur. J. Pharma. Soc., 1999, 9, 25.
4. G. Kanagaraj and G.N. Rao, Indian J. Chem 1993, J. 32 (A), 594.
5. S.A. Tilles, Southern Medical Journal, 2001, 94 (8), 817.
6. C.C. Brachett, Journal of Pharmaco therapy, 2004, 24 (7), 856.
7. H. Singh, V.K. Srivastava, S.N. Shukla, M.K. Srivastava and M.K. Upadhyay, Indian J. Chem., 1994, 33 (A), 350.
8. H.L. Singh, S. Varshney and A.K. Varshney, Appl. Drganomet. Chem., 1999, 13, 637.
9. K. Chaturvedi, R. Chaturvedi and N. Sharma, J. Ind. Chem. Soc., 2006, 83, 269.
10. H.L. Singh, M. Sharma and A.K. Varshney, Synth. React. Met-Org. Chem., 1999, 29, 817.
11. D.M. Adams, Metal ligands and Related Vibrations, 1967, Arnold. London.
12. D.E. Ewing, Org. Magn. Reson., 1999, 12, 499.
13. Shanu Paliwal, Gayatri Kumari and R. Dhakarey, J. Indian Council Chem., 2007, 24 (1), 20.
14. B. T. Cowda and K.M. Usha, Z. Naturforsch, 2002, 57 (A), 967.
15. A. Arona, I. Singh, D. Sud and G. Singh, J. Indian Council Chem, 2002, 20 (1), 19.
16. Harrison's Principles of Internal Medicine, 13th Edn., Mc Graw Hills Inc., 1994, 604.
17. M. Turner, H. Koksal and M.K. Sener, Transition Metal Chemistry, 1999, 24, 414.
18. M. Jain, S. Gaur, V.P. Singh and R.V. Singh, Appl. Organomet. Chem., 2004, 18 (2), 73.