

SYNTHESIS, STRUCTURAL EVALUATION AND BIOLOGICAL ASSAY OF METAL COMPLEXES OF SCHIFF BASES DERIVED FROM SULPHANILAMIDE

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ABSTRACT -Some new Cu (II), Zn (II), Mn (II) and Cr (III) complexes of Schiff bases derived from sulphanilamide have been synthesized. They have been characterized on the basis of elemental analysis, IR and ¹HNMR spectroscopy. 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, biological assay was conducted on the organisms *Escherichia coli*, *Salmonella typhi*, *Bacillus subtilis*, *Staphylococcus aureus*, *Aspergillus flavous*, *Aspergillus niger*, *Penicillium citrinum* and *Fusarium oxysporum*. The result 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 ¹HNMR spectroscopy and biocidal studies.

INTRODUCTION

Sulphanilamide are drugs which show distinct physical, chemical and biological properties.¹⁻³ Many chemotherapeutically important sulpha drugs like sulphadiazine, sulphathiazole, sulphamerazine and sulphonamide possess SO₂NH₂ moiety which has an important toxicophoric function.⁴⁻⁶ The Schiff bases synthesised from the sulpha drug possess pronounced antimicrobial⁷, antitumour⁸⁻⁹, antifouling¹⁰, antioncogenesis¹¹ activities. The condensation products of sulpha drugs with aldehydes and ketones are biologically active and also have good complexing ability; their activity increases complexation with metal ions¹²⁻¹⁵.

The pronounced activity of metal complexes of Schiff bases derived from sulphanilamide has led to considerable interest in their coordination chemistry. A survey of literature reveals that very little attention has been paid on coordination behaviour of Schiff bases derived from sulpha drugs. The newly prepared complexes of sulpha drugs were characterized on the basis of elemental analysis and spectral studies. These complexes were also screened for their fungicidal and bactericidal activities.

EXPERIMENTAL

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

p-Sulphonamidoglucoseanil (SG) was synthesized¹⁶ by refluxing on water bath Sulphonamide (17.2g, 0.1 mole) and Glucose (18.0g, 0.1 mole) in 75 ml alcohol for two hours. On cooling the Schiff base SG 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 prepared¹⁷ by refluxing on water bath, a mixture of 0.01 mole of metal chloride (i.e. 1.70 g of CuCl₂. 2H₂O, 1.36 g of ZnCl₂, 1.97 g of MnCl₂. 4H₂O and 2.66 g of CrCl₃. 6H₂O) in 15 ml ethanol respectively with 0.02 mole of Schiff base SG (i.e. 6.68 g of SG) in 20 ml ethanol for 3 hours. The reaction mixture was concentrated and then cooled. The solid derivatives were separated out. These were filtered, washed and finally air-dried.

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 ¹HNMR spectra of the Schiff base and the metal complexes were recorded in CDCl₃ on a Bruker DRX 300F, 300 MHz FTNMR spectrometer.

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Antibacterial Activity

The bactericidal activity was evaluated by the filter paper disc diffusion method¹⁸. The nutrient agar medium (peptone, beef extract, NaCl and agar-agar) and 5mm diameter paper disc of Whatman No.1 were used. The compounds were 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 37°C and the inhibition zone around each disc was measured.

Antifungal Activity

The fungicidal activity was evaluated by Agar plate technique¹⁹. The fungi were grown in agar medium (glucose 20g, starch 20g, agar-agar 20g and 1000ml water) at $28 \pm 2^\circ\text{C}$ 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 3 days and the percentage inhibition was calculated by the formula.

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

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

RESULTS AND DISCUSSION

The obtained metal complexes of the Schiff base are coloured solid, insoluble in water but soluble in benzene, acetone, DMF and other polar organic solvents. Elemental analyses suggests 1:2 (M : L) Stoichiometry²⁰. All the physical and analytical results are listed in Table-1.

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

COMPOUND	MOL. WT.	COLOUR	M.P. (°C)	ELEMENTAL ANALYSIS %				
				FOUND (CALCULATED)				
				C	H	N	S	METAL
SG [C ₁₂ H ₁₈ O ₇ N ₂ S]	334	White	130°-132°	43.23 (43.11)	5.16 (5.38)	8.22 (8.38)	9.47 (9.58)	- -
Cu-SG [Cu(C ₂₄ H ₃₆ N ₄ O ₁₄ S ₂). 2H ₂ O]	767	Brown	175°C	37.59 (37.54)	5.02 (5.21)	7.44 (7.30)	8.21 (8.34)	8.08 (8.21)
Zn-SG [Zn(C ₂₄ H ₃₆ N ₄ O ₁₄ S ₂). 2H ₂ O]	769	Yellow	190°C	37.39 (37.45)	4.56 (4.68)	7.33 (7.28)	8.45 (8.32)	8.51 (8.45)
Mn-SG [Mn(C ₂₄ H ₃₆ N ₄ O ₁₄ S ₂). 2H ₂ O]	759	Dark Brown	135°C	37.76 (37.94)	5.14 (5.27)	7.29 (7.38)	8.56 (8.43)	7.31 (7.24)
Cr-SG [Cr(C ₂₄ H ₃₆ N ₄ O ₁₄ S ₂). 2H ₂ O]	756	Sea Green	185°C	38.11 (38.09)	5.22 (5.29)	7.56 (7.40)	8.61 (8.46)	6.71 (6.88)

Infra Red Spectra

The Infra red spectra²¹ of the Schiff base and the metal complexes show sharp bands in the region 3250-3300 cm⁻¹ and 1570-1590 cm⁻¹ attributed to the stretching and bending vibrations respectively of $\nu(\text{NH}_2)$. While the symmetric and asymmetric vibrations of $\nu(\text{SO}_2)$ 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 1621cm⁻¹ attributed to $\nu(\text{C}=\text{N})$ azomethine linkage²¹⁻²³, a shift of $\pm 15 \text{ cm}^{-1}$ 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 appear in the region 540-560 cm⁻¹ are tentatively assigned to $\nu(\text{M}-\text{N})$ vibrations. The stretching and bending vibrations found in the region 660-690 cm⁻¹ and 830-860 cm⁻¹ respectively attributed to the coordination of water molecules. The IR-spectral data is tabulated in Table-2.

Table-2. Tentative assignments of some selected bands in the IR spectra (cm⁻¹) of Schiff base (SG) and its metal complexes

Compounds	$\nu(\text{NH}_2)$ (stretch.)	$\nu(\text{NH}_2)$ (bend.)	$\nu(\text{SO}_2)$ (sym.)	$\nu(\text{SO}_2)$ (asym)	$\nu(\text{C}=\text{N})$	$\nu(\text{H}_2\text{O})$ (stretch)	$\nu(\text{H}_2\text{O})$ (bend.)	$\nu(\text{M}-\text{N})$
SG	3374	1599	1146	1312	1639	-	-	-
Cu-SG	3354	1516	1155	1320	1600	667	827	542
Zn-SG	3355	1517	1153	1327	1610	664	828	545
Mn-SG	3426	1568	1154	1341	1623	669	831	540
Cr-SG	3357	1517	1155	1320	1608	666	828	549

¹HNMR Spectra

The ¹HNMR spectra of the Schiff base and its metal complexes show multiplet signals in the region $\delta 6.65-8.40 \text{ ppm}$ due to benzene ring protons. While the signals due to $\text{HC}=\text{N}$ protons²³ appear at $\delta 4.76 \text{ ppm}$ in the spectra of Schiff base while it shifts downfield in the spectra of corresponding metal complexes. Thus, this downfield shift is attributed to the complex formation i.e. attachment of metal with nitrogen atom of $-\text{NH}_2$ group and nitrogen atom^{24, 25} of $\text{HC}=\text{N}$ group. The evidences mentioned above supports the complex formation of the Schiff base. The ¹HNMR data is tabulated in Table-3.

Table-3. ¹HNMR Spectral data of Schiff base (SG) and its metal complexes

S.No.	Compound	Chemical Shift δ (ppm)	Peak position	Group Assigned.
1.	SG	(a) 6.65-7.69 (b) 4.89 (c) 10.02	Multiplet Singlet Singlet	Aromatic ring HC=N -NH ₂
2.	Cu-SG	(a) 6.71 -7.80 (b) 4.96 (c) 10.13	Multiplet Singlet Singlet	Aromatic ring HC=N -NH ₂
3.	Zn-SG	(a) 6.75-7.77 (b) 4.94 (c) 10.14	Multiplet Singlet Singlet	Aromatic ring HC=N -NH ₂
4.	Mn-SG	(a) 6.68-7.66 (b) 4.98 (c) 10.06	Multiplet Singlet Singlet	Aromatic ring HC=N -NH ₂
5.	Cr-SG	(a) 6.79-7.91 (b) 4.92 (c) 10.11	Multiplet Singlet Singlet	Aromatic ring HC=N -NH ₂

On the basis of spectroscopic characterization the tentative structure of metal complexes of Schiff's Base (SG) is given in Figure-1.

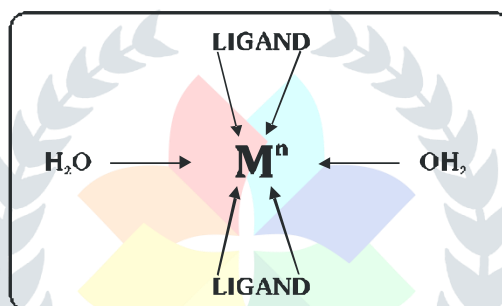


Fig 1: Tentative structure of the metal complexes

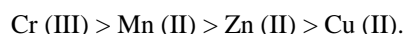
where $M^n = \text{Cu (II)}, \text{Zn (II)}, \text{Mn (II)}$ and Cr (III) metal ions

LIGAND = Schiff Base SG

Antibacterial and Antifungal Activities

The Schiff base (SG) as well as the metal complexes exhibited good amount of activity against all the tested bacteria and fungi. The Schiff base (SG) 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. citrinum*.

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



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. 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. Such chelation increases the lipophilic character of metal chelate, which probably tends to break down the permeability barriers of cells, resulting in the interference with the normal cell process. Thus, the result suggests that the metal complexes of Schiff base (SG) have proved to be excellent bactericides and fungicides in the present investigations.

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