

Synthesis, characterization and biological activity of manganese(II), iron(II), cobalt(II), nickel(II) and copper(II) schiff base complexes against multidrug resistant bacterial and fungal pathogens

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A Schiff base was prepared from the interaction of ethanolic solutions of 2-hydroxy-1-naphthaldehyde and butylenediamine. The complexes were synthesized by refluxing the mixture of ethanolic solutions of the Schiff base and respective metal (II) chloride. Their solubility, melting point/decomposition temperature, molar conductance, elemental analysis and IR were carried out. The melting point of the Schiff base and the decomposition temperature of the complexes determined are high. The Schiff base and its metal (II) Schiff base complexes are insoluble in water and most common organic solvents, except methanol, ethanol and DMSO. The molar conductance of the complexes determined falls in the range 9 – 12 Ohm⁻¹cm²mol⁻¹. Elemental analysis of the complexes for C, N and H revealed 1:1 metal to Schiff base ratio. The IR spectral analysis of the free Schiff shows a band at 1641 cm⁻¹, which is assigned to $\nu(\text{C}=\text{N})$ stretching vibrations. This band is observed in the complexes but at lower frequencies, indicating coordination of the Schiff base to the metal ion through the azomethine group. The Schiff base and its divalent metal complexes were screened for their antibacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris* and *Salmonella typhi* as well as *Rhizopus nigricans*. and *Mucor specie* fungal isolates. It has been found that all the complexes show different activity on the isolates and that the complexes show higher activity than the free ligand.

Keywords: Schiff base, butylenediamine, 2-hydroxy - 1 - naphthaldehyde, antibacterial, antifungal, complex, isolates.

INTRODUCTION

A Schiff base (or azomethine), named after Hugo Schiff (1864) is a nitrogen analogue of an aldehyde or ketone in which the C=O group is replaced by a C=N carbon – nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group, but not hydrogen. They are usually obtained by the condensation of an aldehyde or ketone with primary amine (Holm *et al.*, 1966). Schiff bases are of the general formula $R_1R_2C = NR_3$, where R_3 is an aryl or alkyl group that makes the Schiff base a stable imine (Henry

and Lange, 1977). Transition metal Schiff base complex compounds are well known, for example, Ettling (1840) isolated a dark green crystalline product from the reaction of cupric acetate, salicylaldehyde and aqueous ammonia (Holm *et al.*, 1966). However, there was no comprehensive and systematic study until the preparative work of Pfeiffer and associates (1931), who reported a series of complexes derived from Schiff bases of salicylaldehyde and its substitution products. Recently, Gupta *et al.* (2002) reported the synthesis and characterization of cobalt (II) N, N' - bis(acetylaceton)ethylenediiminato complex from the interaction of cobalt (II) salt and N, N' - bis(acetylaceton)ethylenediimine Schiff base ligand. In another report, Xishi *et al.* (2003) described the

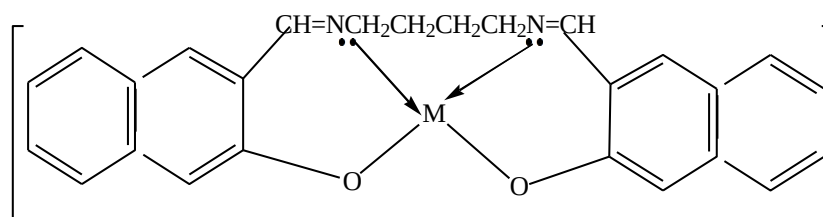


Figure 1. The proposed molecular structure of the metal (II) schiff base cpmplexes where M is Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} or Cu^{2+}

synthesis and spectroscopic properties of manganese (II), cobalt (II) and copper (II) complexes with novel Schiff base ligand derived from 2, 2' bis(p-methoxyphenylamine) and salicylic aldehyde.

Transition metal Schiff base complexes are characterized by important properties such as antitumor, anti fertility, bioactivity and catalytic activity. For example, some Schiff bases and their metal complexes containing Co(II), Ni(II), Cu(II) and Zn(II) synthesized from salicylaldehyde, 2, 4 - dihydroxybenzaldehyde, glycine and L-alanine possess antitumor activity (Gaowen et al., 1995). The complexes formed by Schiff bases derived from hydrazine carboxamide and hydrazine with dioxo Mo(IV) and Mn(II) have been reported to alter reproductive physiology (Singh et al., 1999). Schiff base derived from furylglyoxal and p-toluidene shows antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Proteus vulgaris* (Bhardwaj and Singh, 1994). As catalysts, iron (II) Schiff base complex exhibits catalytic activities towards electro-reduction of oxygen (Chakraborty et al., 1994).

This paper reports synthesis, physicochemical characterization and biological activity of manganese(II), iron(II), cobalt(II), nickel(II) and copper(II) Schiff base complexes

EXPERIMENTAL

All chemicals and solvents used were of analytical grade (AnalaR or BDH) while butylenediamine and 2-hydroxy-1-naphthaldehyde were obtained from Sigma-Aldrich and were used without further purification. Molar conductance measurements were carried out using Jenway 4010 conductivity meter. Elemental analyses for carbon, nitrogen and hydrogen were carried out at the Micro-analytical Laboratory at the University of Bristol, United Kingdom. Four pathogenic bacteria viz: *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus vulgaris* and *Salmonella typhi* and two fungi *Rhizopus nigricans* and *Mucor specie* were collected from Microbiology unit of the Department of Biological Sciences, Bayero University, Kano, Nigeria. Nutrient agar and Potato Dextrose agar were used as bacteriological and fungal media respectively.

Preparation of the Schiff Base

A solution of 0.1 mole butylenediamine in 50cm³ ethanol was slowly added to a solution of 0.2 mole 2 - hydroxy - 1 - naphthaldehyde in 50cm³ ethanol. The mixture was refluxed for an hour. The Schiff base that formed was filtered and washed with ethanol and dried over phosphorus pentoxide for a week (Ahmed and Akhtar, 1983; Byeong-Goo et al., 1996).

Preparation of the complexes

All the N, N' bis(2-hydroxy-1-naphthyl) butylenediiminato metal (II) complexes were prepared by addition of the mixture of Schiff base (0.01 mole) and sodium hydroxide (0.02 moles) in hot ethanol (100cm³) into an aqueous solution of a metal (II) chloride (0.01 mole). The mixture was refluxed for 2 hours. The metal (II) Schiff base complex that formed was separated, washed with ethanol and dried over phosphorus pentoxide for a week (Ahmed and Akhtar, 1983; Byeong-Goo et al., 1996).

Antibacterial and Antifungal Activity Tests

The N, N' bis(2-hydroxy-1-naphthyl) butylenediiminato (Schiff base) and its divalent metal complexes were dissolved separately in DMSO to have three different concentrations (500µg, 1000µg and 2000µg) per disc. They were placed on the surface of the culture and incubated at 37°C for 24hrs (Ramon et al., 2003; Yeamin et al., 2003). The *in vitro* antibacterial activity was carried out by disc diffusion method. The diameter of zone of inhibition produced by the Schiff base and its metal (II) complexes were compared with Augumentin (30µg) and Ketoconazole (600µg) for bacterial and fungal standard respectively.

RESULTS AND DISCUSSION

The Schiff base prepared is powdery yellow solid, with percentage yield 79.8% and melting point of 263°C. The color of Fe(II), Co(II) and Ni(II) Schiff base complexes is

Table 1. Physical properties of the Schiff base and its metal (II) complexes

Ligands/Complexes	Colour	% Yield	MeltingPoint (°C)	Decomposition (°C)	Temp.
Ligand	Yellow	79.84	263	-	
[MnL]	Green	64.84	-	340	
[FeL]	Brown	74.37	-	330	
[CoL]	Brown	82.62	-	340	
[NiL]	Red	71.18	-	341	
[CuL]	Blue	71.19	-	344	

L = N, N' - bis (2-hydroxy-1-naphthyl)propylenediiminato

[MnL] = N, N' - bis (2-hydroxy-1-naphthyl)butylenediiminato manganese (II)

[FeL] = N, N' - bis (2-hydroxy-1-naphthyl)butylenediiminato iron (II)

[CoL] = N, N' - bis (2-hydroxy-1-naphthyl)butylenediiminato cobalt (II)

[NiL] = N, N' - bis (2-hydroxy-1-naphthyl)butylenediiminato nickel (II)

[CuL] = N, N' - bis (2-hydroxy-1-naphthyl)butylenediiminato copper (II)

Table 2. Solubility of the Schiff base in water and common organic solvents

Solvent	Ligand	[MnL]	[FeL]	[CoL]	[NiL]	[CuL]
Water	IS	IS	IS	IS	IS	IS
Methanol	S	S	S	S	S	S
Ethanol	S	S	S	S	S	S
Ether	IS	IS	IS	IS	IS	IS
Acetone	S	S	S	S	S	S
Nitrobenzene	SS	SS	SS	SS	SS	SS
Acetonitrile	SS	SS	SS	SS	SS	SS
Carbon tetrachloride	IS	IS	IS	IS	IS	IS
Dimethylsulphoxide	S	S	S	S	S	S

S – Soluble

IS – Insoluble

SS – Slightly Soluble

Table 3. Molar conductance of the metal (II) Schiff base complexes

Complex	Electrical conductance (ohm ⁻¹ cm ²)	Molar conductance (ohm ⁻¹ cm ² mol ⁻¹)
[MnL]	11×10 ⁻⁶	11.00
[FeL]	10×10 ⁻⁶	10.00
[CoL]	9×10 ⁻⁶	9.00
[NiL]	12×10 ⁻⁶	12.00
[CuL]	10×10 ⁻⁶	10.00

brown while, Mn(II) and Cu(II) complexes are green and blue respectively. The decomposition temperature of manganese (II), iron (II), cobalt (II), nickel (II) and copper (II) complexes are 340, 330, 340, 341 and 344°C respectively, indicating good stability (Table 1). Solubility test carried out on the Schiff base and its divalent metal complexes in water and some common solvents showed that they are soluble in methanol, ethanol and DMSO but insoluble in water, ether and carbon tetrachloromethane (Table 2). The molar conductance values of the metal (II) Schiff base complexes determined in 10⁻³M DMSO solution are in the range 9 -12 ohm⁻¹cm²mol⁻¹, these values are very

low (Table 3), suggesting that they are non-electrolytes (Geary, 1971).

The elemental analysis of the Schiff base and its divalent chelates for H, C and N determined showed that the observed and the calculated percentages of the elements are in good agreement and the result suggested 1:1 metal-Schiff base ratio in all the complexes (Table 4).

The infrared spectra of the Schiff base showed a broad band at 3418 cm⁻¹ which is assigned to ν(O-H) stretching vibrations. This band was absent in all the complexes, revealing deprotonation on coordination of the Schiff base to the respective metal (II) ion (Ahmed

Table 4. Elemental Analysis Results of the metal(II) Schiff base complexes

Compound	% Calculated (found)		
	C	H	N
Ligand	78.86(78.48)	6.11(6.10)	7.07(7.01)
[MnL]	64.21(64.21)	4.94(4.80)	6.24(6.01)
[FeL]	64.08(64.08)	4.93(4.90)	6.23(5.98)
[CoL]	63.64(63.55)	4.90(4.45)	6.18(6.01)
[NiL]	63.68(62.89)	4.90(4.65)	6.19(6.16)
[CuL]	63.00(62.99)	4.85(4.58)	6.12(6.05)

Table 5. IR of the Schiff base and its metal (II) Complexes

Compound	ν (O—H) (cm ⁻¹)	ν (C=N) (cm ⁻¹)	ν (M—O) (cm ⁻¹)	ν (M—N) (cm ⁻¹)
Ligand	3418	1641	-	-
[MnL]	-	1589	574	751
[FeL]	-	1620	508	751
[CoL]	-	1630	525	719
[NiL]	-	1630	593	752
[CuL]	-	1604	517	717

Table 6. Sensitivity of bacterial (clinical) isolates to metal (II) Schiff base complexes

Isolates	[MnL]			[FeL]			[CoL]			[NiL]			[CuL]		
	500	1000	2000	500	1000	2000	500	1000	2000	500	1000	2000	500	1000	2000
<i>E. coli</i>	NZI	10	10	NZI	NZI	NZI	8	9	9	NZI	NZI	NZI	NZI	NZI	NZI
<i>Kleb</i>	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI	NZI
<i>Proteus</i>	8	9	9	9	9	9	10	10	10	7	8	8	NZI	NZI	NZI
<i>Salmonella</i>	10	10	10	7	8	9	8	9	10	7	7	7	NZI	NZI	NZI

KEY: NZI = No zone of inhibition

and Akhtar, 1983). The strong peak at 1641 cm⁻¹ in the free Schiff base was attributed to azomethine ν (C=N) vibration frequencies, which was in agreement with Byeong-Goo *et al.* (1996). However, this band was observed to shift to the lower frequencies in all the metal (II) Schiff base complexes, suggesting the participation of azomethine nitrogen of the Schiff base on coordination to the respective metal ions (Ahmed and Akhtar, 1983). The absorption bands in the ranges 717 – 752 cm⁻¹ and 508 – 593 cm⁻¹ observed in all the complexes were assigned to ν (M—N) and ν (M—O) vibrational frequencies, respectively, confirming coordination of the Schiff base to the respective metal ions (Table 5).

The antibacterial activity tested for the Schiff base and all the metal (II) schiff base complexes have been determined. The diameter of inhibition zone (mm) was measured for each treatment. *Klebsiella pneumoniae* is found to be resistant to the Schiff base at all concentrations; *E. coli* is active on the Schiff base. The result for *Proteus vulgaris* showed minimal activity against the organism at all concentrations. The cobalt (II) Schiff base complex showed strong activity on the

isolates, while nickel (II) and copper (II) showed no activity on all the isolates, however, iron (II) and manganese (II) complexes showed some activity on *Proteus vulgaris* and *Salmonella typhi* but each has no activity on *E. coli* and *Klebsiella pneumoniae*. The results are shown on Table 6.

Sensitivity of fungal isolates (*Mucor specie.* and *Rhizopus nigricana*) showed that the Schiff base is active on both the isolates at all concentrations. The result for *Mucor specie* and *Rhizopus nigricans* showed maximal activity against the organism at all concentrations for all the complexes except that of nickel, which showed no activity (Table 7). In general, the results indicate that the complexes show more activity than the Schiff base under similar experimental conditions. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane and can be explained by Tweedys chelation theory (Fehmi *et al.*, 1998). Chelation considerably reduces the polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible electron delocalization over the whole chelate ring. Such chelation could also enhance

Table 7. Sensitivity of fungal isolates to metal (II) Schiff base complexes

Isolates	[MnL]			[FeL]			[CoL]			[NiL]			[CuL]		
	500	1000	2000	500	1000	2000	500	1000	2000	500	1000	2000	500	1000	2000
<i>Rhizopus sp</i>	15	16	17	12	15	12	10	15	10	6	6	6	8	10	10
<i>Mucor sp</i>	11	12	12	8	10	10	6	8	12	6	6	6	7	8	11

E. coli = *Escherichia coli*
Kleb = *Klebsiella pneumonia*
Proteus = *Proteus vulgaris*
Salmonella = *Salmonella typhi*
Rhizopus sp = *Rhizopus nigricans*
Mucor sp = *Mucor specie*

the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane (Tuner et al., 2007).

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