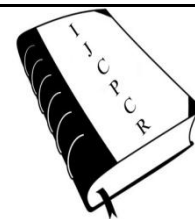




International Journal of Current Pharmaceutical & Clinical Research



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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF SOME TRANSITION METAL COMPLEXES WITH A NEW MANNICH BASE

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ABSTRACT

A new Mannich base, N-(1-Morpholinesalicylyl)semicarbazide (MSS), formed by the condensation of morpholine, semicarbazide and salicylaldehyde and its Cu(II), Ni(II), Co(II) and Zn(II) complexes have been synthesised. Their structures have been elucidated on the basis of analytical, magnetic, electrical conductivity and spectral methods. The electrochemical property of the ligand and its complexes in acetonitrile solution was studied by cyclic voltammetry. The X-band ESR spectra of the Cu(II) complex in DMSO at 300 and 77 K were recorded and their salient features are reported. Based on this data, we propose an octahedral geometry for Cu(II), tetrahedral geometry for Co(II) and Zn(II) and square planar geometry for Ni(II) complexes. Antibacterial activities of the ligand and its complexes were tested against some selected bacteria. The ligand and all the complexes showed antimicrobial activities.

Key words: Morpholine, Salicylaldehyde, Metal complexes, Spectral studies, Antimicrobial activity.

INTRODUCTION

Metal complexes of Mannich bases have been studied [1-5] extensively in recent years due to selectivity and sensitivity of the ligand towards various metal ions. From the survey of existing literature, it appears that metal complexes of Mannich base have played a vital role in the development of coordination chemistry [6-10]. A search through the literature reveals that no work has been done on the condensation of morpholine, salicylaldehyde and semicarbazide. It is well known from the literature that semicarbazide compounds containing the amide moiety have a strong ability to form metal complexes. In the present work, a new Mannich base derived from the condensation of morpholine, salicylaldehyde and semicarbazide and its metal complexes with Cu(II), Co(II), Ni(II) and Zn(II) were synthesized and characterized using different physicochemical techniques. The ligand and its metal complexes have biological activities against various microbes such as *Bacillus subtilis* *staphylococcus aureus*,

pseudomonas aeruginosa, *Escherichia coli*, *candida albicans* and *Aspergillus niger*.

MATERIALS AND METHODS

Chemicals

Reagents such as morpholine, salicylaldehyde, semicarbazide and various Metal(II) chlorides were of Merck products. The melting points of all compounds were determined in open capillaries and are uncorrected. Purity of the compound was checked by TLC using Silica gel G coated glass plates with chloroform and ethyl acetate (1:1) as eluent and iodine vapour as visualizing agent and confirmed by retention factor (R_f) value. The IR spectra were recorded in KBr pellets using FT-IR shimadzu IR affinity 1. The ¹H NMR and ¹³C NMR Spectra were recorded on Bruker AMX400 NMR spectrophotometer using TMS as internal standard and chemical shifts were

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expressed in ppm. The elemental analysis were performed on Perkin Elmer Series C, H, N & S analyser 2000. Mass Spectra were recorded on a JEOL – 8X 102. UV-visible spectra of the complexes were recorded on Perkin Elmer Lambda EZ201 spectrophotometer in DMF solution. Molar conductivity was determined using Systronic Conductivity Bridge with a dip type cell using 10^{-3} M solution of complexes in DMSO. Cyclic voltammogram of the complexes were recorded in acetonitrile solution at 300 K using a three-electrode cell comprising reference Ag/AgCl, auxiliary Pt and working glass carbon electrodes. Magnetic susceptibility measurements of the complexes were done using a Gouy balance. The ESR spectral studies were made in JEOL-DPS-2000.

Synthesis of Mannich base

In a typical procedure [11], an ethanolic solution of salicylaldehyde, morpholine and semicarbazide were taken in 1:1:1 mole ratio. Morpholine 4.4 mL (0.05 mol), semicarbazide 6.7 g (0.05 mol) and 6.1 mL of salicylaldehyde (0.05 mol) were mixed and continuously stirred for 3 hours under ice-cold condition. The yellow coloured solid (fig-1) formed was filtered and recrystallized using methanol. The purity of the compound was checked with TLC. The melting point of the recrystallized sample was recorded. Yield: 63%, m.p. 212 °C.

Synthesis of metal complexes

The mannich base (dissolved in CHCl_3) and the metal chlorides in ethanol were mixed in 1:1 molar ratio. The reaction mixture was gently warmed on a water-bath for one hour. The resulting solution was concentrated to a third of its volume and cooled to 0 °C for 6 hours. The precipitated complexes were filtered, washed with ethanol and dried in vacuo. The proposed structures of the complexes are given in Fig-2.

Antibacterial activity

The *in vitro* biological screening effects of the synthesized Mannich base and its Cu(II), Co(II), Ni(II) and Zn(II) complexes have been studied for their antibacterial and antifungal activities by disc diffusion method at concentration of 10 µg / ml in DMSO using both gram positive *S.aureus*, *B.Subtilis*, gram negative *E.Coli*, *P.Aeruginosa* and antifungal activity against *C.albicans* and *A.niger*. The zone of inhibition was measured in mm and the activity was compared with Ciprofloxacin 1µg/disc for bacteria and Nystatin 10µg / disc for fungi as standard drugs. The compounds possess appreciable antibacterial activities against selected organisms but lesser when compared with their standards. The zone of inhibition values are presented in Table-2.

RESULT AND DISCUSSION

The elemental analyses show 1:1 (Metal: Ligand) stoichiometry for all the complexes. The analytical data of the ligand and the complexes are given in Table 1. They correspond well with the general formula ML , where $\text{M} = \text{Cu(II)}$, Ni(II) , Co(II) and Zn(II) ; $\text{L} = (\text{C}_{12}\text{H}_{18}\text{N}_4\text{O}_3)$. The low conductance of the chelates supports the non-electrolytic nature of the metal complexes.

Infrared spectra

The IR spectra of the Mannich base ligand (MSS) and its complexes are recorded. The IR spectra of the complexes were compared with those of the free ligand in order to determine the coordination sites that may be involved in coordination. In MSS, the infrared bands observed at 3159, 1690 and 1267 cm^{-1} have been assigned to $\nu_{\text{N-H}}$ amide, $\nu_{\text{C=O}}$ and $\nu_{\text{C-N-C}}$ of morpholine group respectively. In IR spectra of all the complexes, the $\nu_{\text{N-H}}$ band remained at the same position as in the free ligand, indicating that the secondary nitrogen is not coordinated. A band due to $\nu_{\text{C-N-C}}$ of the morpholine ring appearing at 1267 cm^{-1} in the metal complex remained at the same position as in the free ligand indicating that the nitrogen atom from the morpholine ring is not coordinated. A band due to $\nu_{\text{N-H}}$ adjacent to methyne carbon have stretching vibration appearing at 1148 cm^{-1} in the ligand is shifted to 1126 cm^{-1} in the metal complex, suggesting the coordination of the nitrogen atom adjacent to methyne carbon to central metal ion. It is observed that the band appearing at 1690 cm^{-1} due to $\nu_{\text{C=O}}$ in the ligand is shifted to 1658 cm^{-1} in the metal complex indicating the involvement of carbonyl oxygen in coordination. The new bands at 496 and 472 cm^{-1} in the spectra of the metal complexes were assigned to $\nu_{\text{M-O}}$ and $\nu_{\text{M-N}}$ stretching vibrations [12-15]. The Presence of coordinated water molecules in Cu(II) complex is determined by the appearance of bands at 3200-3400 cm^{-1} and a peak at 863 cm^{-1} is assignable to the OH stretching and rocking mode of coordinated water molecules. The rocking vibration of water is not observed in the IR spectra of Ni(II), Co(II) and Zn(II) complexes. This is confirmed that water molecule is not coordinated in these complexes.

Magnetic moment and UV-Visible spectra

Electronic spectra and magnetic measurements were recorded in order to obtain information about the geometry of the complexes. The μ_{eff} (1.9 BM) value of the Cu(II) represents an octahedral geometry of the ligand around the central metal ion. The four coordinated Co(II) complex shows μ_{eff} value of 3.6 BM which indicates the presence of three unpaired electrons and it supports the tetrahedral geometry. The observed zero magnetic moment value confirms the square planar environment for the Ni(II).

The Zn(II) complex is found to be diamagnetic as expected for d^{10} configuration.

The electronic spectra of the ligand and its complexes were recorded in DMSO solution. The Cu(II) ion with d^9 configuration in a complex can be either octahedral or tetrahedral or rarely square planar. The octahedral coordinated Cu(II) ion has the ground state ${}^2E_g(t_{2g})^6(e_g)^3$. The only excited state should then be ${}^2T_{2g}(t_{2g})^5(e_g)^4$, the energy difference being 10 Dq. The Cu(II) complex under the present study exhibits a broad band in the region 12720 cm^{-1} . The broadness of the band may be due to Jahn-Teller distortion [16,17]. This observation indicates that the complex has distorted octahedral structure. Co(II) complex displays a band at 15655 cm^{-1} which is assigned to ${}^4A_2 \rightarrow {}^4T_1$ for tetrahedral geometry [18]. The Ni(II) complex is diamagnetic suggesting a square planar geometry [19]. It showed a broad band at 14588 cm^{-1} which is assigned to ${}^1A_{1g} \rightarrow {}^1B_{1g}$. The spectrum of this complex is consistent with this assignment. No transitions were observed in the visible region for the Zn(II) complex consistent with the d^{10} configuration of the Zn^{2+} ion. This complex is also found to be diamagnetic as expected for d^{10} configuration.

ESR, 1H -NMR and ${}^{13}C$ -NMR spectra

The EPR spectrum of the Cu(II) complex shows $g_{\parallel} > g > 2.0023$ and a g value within the range of 2.08-4.49 is consistent with the $d_{x^2-y^2}$ ground state in an octahedral geometry. Evidence for the bonding mode of the ligand is also provided by the 1H -NMR spectra of the Mannich base and the diamagnetic Zn(II) complex, which were recorded in $CDCl_3$. The 1H -NMR spectrum of the MSS displayed the following signals: a multiplet at 7.3-7.4 δ (Ar-H), 6.5 δ (d, H, NH), 4.8 δ (q, H, NH), 7.7 δ (d, H, CH), 2.5 δ (morpholine N- CH_2), 3.4 δ (morpholine O- CH_2) and 7.8 δ (s, 2H, NH_2). The peak at 10.2 ppm is attributed to the phenolic -OH group present in salicylaldehyde. The presence of this peak, noted for Zn(II) complex, confirms that the -OH proton is free from complexation. In Zn(II) complex, the doublet of the N-H proton is shifted slightly down field to 6.9 δ and it reveals the coordination of carbonyl oxygen to Zn(II) ion. The signal due to ν_{N-H} adjacent to methyne carbon is also slightly shifted downfield and appeared at 4.2 δ in the complex. This is

an indication of the coordination of the nitrogen atom adjacent to methyne carbon to central metal ion. Therefore, it is concluded that the Mannich base behaves as a neutral bidentate ligand in all the complexes.

In the ${}^{13}C$ -NMR spectrum the amide C=O carbon appears at 158 ppm. The signal observed between 137.35 - 126.61 ppm is due to aromatic CH- carbon and 116 ppm for N-CH carbon. The signals due to the O(CH_2) $_2$ and N(CH_2) $_2$ carbons of Morpholine are obtained at 40 and 38 ppm respectively.

Electrochemical Study

The Cu(II) complex exhibited two quasi-reversible peaks. A cyclic voltammogram of Cu(II) displays two reduction peaks, first one at $E_{pc} = -0.65\text{ V}$ with an associated oxidation peak at $E_{pa} = -0.5\text{ V}$ and second reduction peak at $E_{pc} = -1.58\text{ V}$ with an associated oxidation peak at $E_{pa} = -1.8\text{ V}$ corresponding to the Cu(II) / Cu(I) and Cu(I) / Cu(0) respectively at a scan rate of 0.2 V/s. The value of ΔE_p are 1.5 and 2.02 for first and second redox couples respectively and increase with scan rate giving evidence for quasi-reversible nature associated with one electron reduction.

Antimicrobial study

For *in vitro* antimicrobial activity, the synthesized compounds were tested against the bacteria *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* and fungi *Candida albicans* and *Aspergillus niger* [20,21]. The minimum inhibitory concentration (MIC) values of the investigated compounds with the standard drugs are presented in Table.2. Antimicrobial activity of metal chelates can be explained on the basis of chelation theory [22]. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of charge of the metal ion with donor groups. Further, it increases the delocalization of π - electrons over the whole chelate ring and enhances the presentation of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganism. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism.

Table 1. Physical Characterization, Analytical, molar conductance, Magnetic susceptibility data

Comp ound	Colour	Found/(Calculated)					Mol. W t	Yiel d %	λ_m $\Omega^{-1}\text{ cm}^2$ Mol $^{-1}$	μ_{eff} BM
		M%	C%	H%	N%	Cl %				
$C_{12}H_{18}N_4O_3$	Colourless	-	56.12(42.89)	5.96(6.35)	13.08(14.04)	-	266	63	-	-
Cu (II) compl ex	Green	16.05(16.10)	33.02(33.12)	5.04(5.15)	12.84(12.92)	14.67	436	60	2.9	1.9

Co (II) complex	Pink	15.38(15.45)	36.92(37.05)	4.61(4.72)	14.35(14.52)	16.41	390	59	4.5	3.6
Ni (II) complex	Pale green	16.66(16.75)	36.36(36.42)	4.54(4.62)	14.14(14.27)	16.16	396	55	2.1	-
Zn (II) complex	Colourless	17.91(18.04)	35.82(35.94)	4.47(4.53)	13.93(14.07)	15.92	402	62	3.4	-

Table 2. Antimicrobial Activities of Metal Complexes of MSS

Compound	Diameter Zone of Inhibition (mm)					
	Gram Positive		Gram Negative		Fungi	
	<i>S.aureus</i>	<i>B.Subtilis</i>	<i>E.Coli</i>	<i>P.aeruginosa</i>	<i>C.albicans</i>	<i>A.niger</i>
MSS	23	20	20	18	17	18
Cu(II)	20	18	15	17	13	15
Co(II)	20	17	18	16	12	16
Ni(II)	22	21	19	17	17	19
Zn(II)	21	20	20	18	18	17
Standard	29*	32*	28*	30*	33**	32**
DMSO (Solvent)	NI	NI	NI	NI	NI	NI

NI= No Inhibition * Ciprofloxacin ** Nystatin

Figure 1. Formation of Mannich base

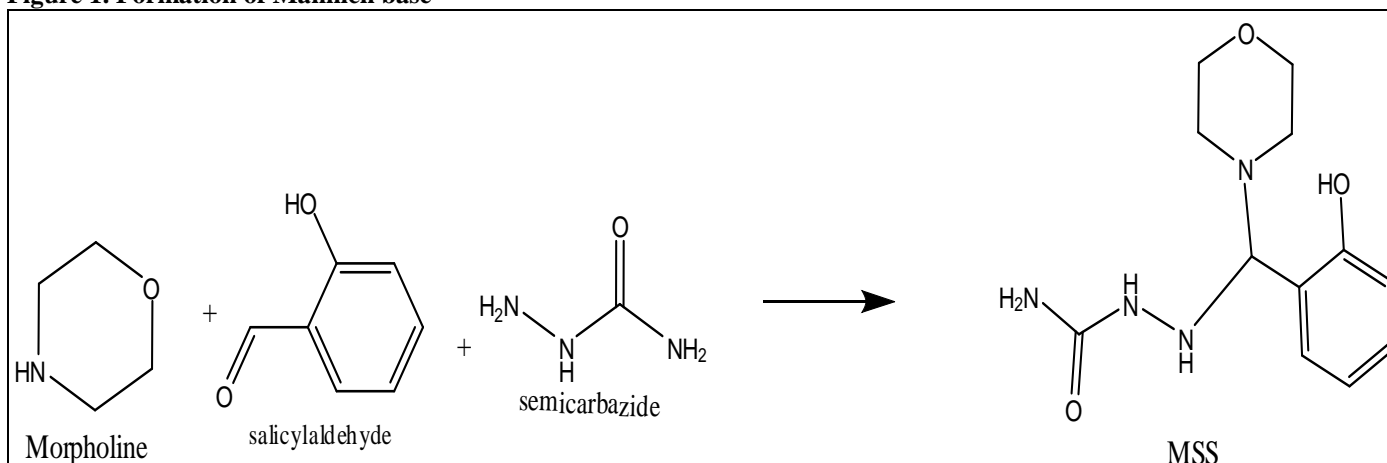
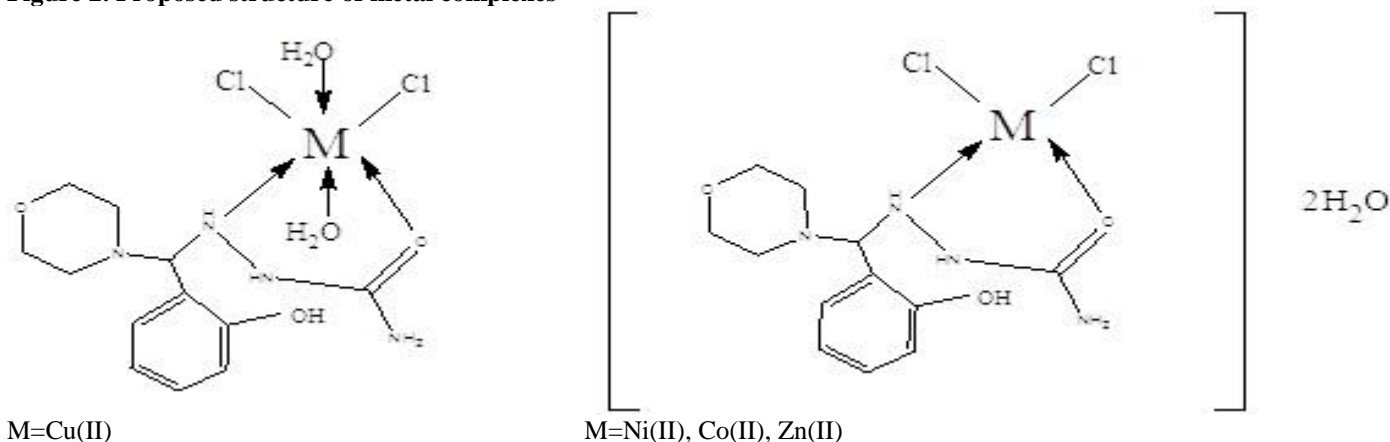


Figure 2. Proposed structure of metal complexes



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