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Synthesis, characterization biological studies of new bis mannich base and its transition metal complexes

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ABSTRACT

Synthesized a new mannich base and its transition metal complexes. These are characterized by using UV, IR, ^{1}HNMR, ^{13}CNMR spectroscopic techniques and their physical data such as melting point, magnetic susceptibility, molar conductance. Antibacterial screening of newly synthesized compounds was carried out against E. coli, P. aureoginosa (gram negative) S. aureus, staphylococcus epidermidis (gram positive) and antifungal activity against C. albicans and A. niger according to disc diffusion method. The transition metal complexes showed good antibacterial and antifungal activity than the free ligand which was explained on the basis of chelation theory.

Keywords: Transition metal complexes, Mannich base, Antibacterial activity, Antifungal activity.

1. INTRODUCTION

Organic chelating agents containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit a variety of biological activities such as antibacterial, antifungal, anti T.B activity, anti HIV activity, antiviral, antiulcer, anti-hypertensive[1-7].The number of studies have been done in the various mannich base complexes formed by the condensation of secondary amines with different aldehydes and amides[8-11]. From the survey of existing literature, it appears that metal complexes of mannich bases played a vital role in the development of coordination chemistry and their analytical utility in the determination of both transition and non transition metal ions is well established. Literature studies revealed that during the past decades, there has been a great deal of interest in the synthesis and structural elucidation of transition metal complexes containing amide moiety. However, there is no study on any metal complexes of N,N'-(piperazine-1,4-dibis((2-hydroxyphenyl)methylene)) diacetamide. In the present work, we described synthesis, characterization and biological studies of new mannich base N,N'-(piperazine-1,4-dibis((2-hydroxyphenyl)methylene)) diacetamide derived from the condensation of salicylaldehyde, piperazine, acetamide and its metal complexes obtained with Cu (II), Ni (II), Co (II) and Zn (II) metals.

2. MATERIAL AND METHODS

2.1. General

All the chemicals used were of reagent grade and purchased from loba, Sigma-Aldrich and E. Merck. All the chemicals were used without further purification and progress of the reaction was monitored by using TLC technique where hexane and ethylacetate used as eluents. Molar conductance were measured in DMF solvents at room temperature. Magnetic susceptibilities were measured at room temperature on a Gouy balance by using $CuSO_4$ as standered. IR spectra (KBr) were recorded on Perkin-Elmer FT-IR spectrophotometer. The electronic spectra were recorded in DMSO on on Shimazdu UV mini-1240 spectrophotometer. The antibacterial and antifungal activities of both ligand and its metal complexes were studied by disc diffusion method against Pseudomonas aeruginosa, Escherichia coli, (gram negative*),* Staphylococcus aureus, staphylococcus epidermidis (gram positive) and aspergillus niger, candida albicans (fungus).

2.2. Synthesis of ligand

To the ethonalic mixture of salicylaldehyde (1 equivalent) and acetamide(1 equvalent) were kept in ice cold condition, piperazine (1 equivalent) was added slowly with constant stirring. This reaction mixture was stirred 30-45 minutes, the yellow colour product formed was kept aside for 20 minutes. The mother liquid was decanted and the solid formed was poured in ice cold water to remove the unreacted acetamide and pipperazine. The progress of reaction was moniterd by TLC where 7:3 hexane and ethylacetate used as eluents. Yield:72%, Mp:160-165^{o}C.

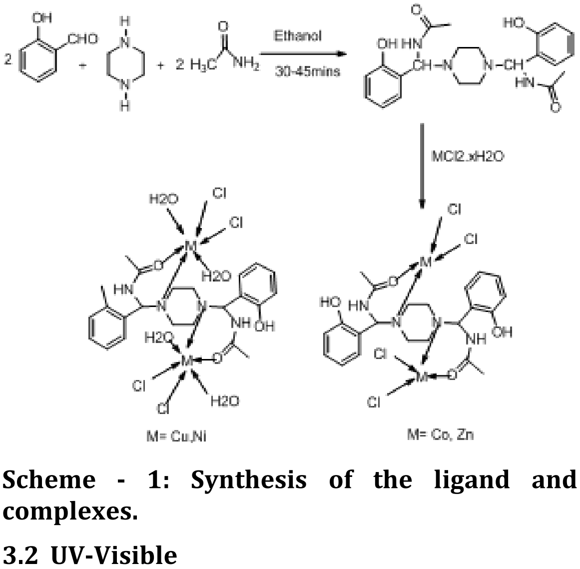
2.3. Synthesis of complexes

Hot ethanolic solution of corresponding metal chlorides (2 equivalent) was slowly mixed with hot ethanolic solution of the respective ligand (1 equivalent) with constant stirring. The mixture was refluxed for 1-2 hours at 60-70^{o}C and on cooling the contents, the colored complex separated out in each case. It was filtered and washed with 50% ethanol and dried.

3. RESULTS AND DISCUSSION

3.1. Molar conductance and Magnetic moment

The complexes prepared were various coloured, powder like, air stable, partially soluble in ethanol, methanol, chloroform and soluble in dimethylformamide (DMF) and dimethylsulfoxide (DMSO). The analytical data and some physical properties of the metal complexes are listed in table 1 and synthetic scheme of complex is given in scheme 1. The molar conductivities showed that all the complexes are non-electrolytes nature with Λm = 1.7-4.0 $\Omega^{-1}cm^{2}mol^{-1}$in 10^{-3} in DMF solutions at room temperature. The *μeff* (1.8) value of the Cu(II) representing an octahedral geometry of the complex around the central metal ion. The four coordinated Co (II) complex showed μeff value of 3.8 which indicates the presence of three unpaired electrons, supports tetrahedral geometry. The observed *μeff* (2.7) value of the Ni (II) confirmed octahedral geometry. The Zn (II) complex is found to be diamagnetic as expected for d^{10} configuration and squar planar geometry.



Scheme - 1: Synthesis of the ligand and complexes.

3.2 UV-Visible

The Cu (II) complex under the present study exhibits a broad band in the region 26315 cm^{-1}.due to transition between $^{2}Eg \rightarrow {}^{2}Tg$ which indicated octahedral geometry. Co (II) complex displays a bands at 25600 cm^{-1} and 30115 cm^{-1} were assigned to $^{4}A_{2} \rightarrow {}^{4}T_{1}$ and $^{4}A_{2} \rightarrow {}^{4}T_{2}$ transitions supported tetrahedral geometry. The Ni (II) complex showed a broad bands at 25773cm^{-1} and 30303 cm^{-1} which is assigned to $^{3}A_{2g} \rightarrow {}^{3}T_{1g}$ and $^{3}A_{2g} \rightarrow {}^{3}T_{2g}$ transition respectively confirmed the octahedral geometry. The spectra of Zn (II) complex exhibited band assigned to L → M charge transfer and not for d-d transition (Figure -1).

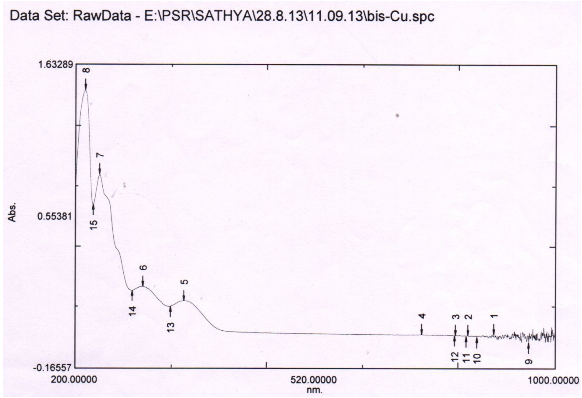


Figure - 1: UV-Visible spectra of Cu(II) complex in DMSO solvent.

3.3. IR-Spectroscopy

The infrared bands of ligand observed at 3252, 1653 and 1155 cm^{-1} have been assigned to **ν**N-H, **ν**C=O and **ν**C-N-C of piperazine group respectively. In IR spectra of all the complexes, the **ν**N-H band remained at the same position as in the free ligand, indicating that the secondar nitrogen is not coordinated. A band due to *νC–N–C* and amide oxygen in all the complexes shifted towards lower frequency clearly indicated coordination of these groups with metal (see table-2). The new bands at 512-544 cm^{-1} and 427-477 cm^{-1}in the spectra of the metal complexes were assigned to *ν*M–O and νM–N stretching vibrations. The

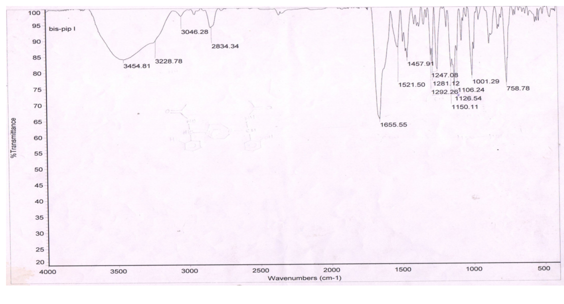


Figure - 1: FT- IR Spectra of ligand using KBr pellets.

presence of coordinated water molecule in Cu (II) and NI(II) complex is determined by the appearance of bands at 3400-3300 cm^{-1} and a peak at 850 cm^{-1}assignable to the OH stretching and rocking mode of coordinated water molecules and these bands are absent in Mn(II) and Zn(II) complexes.

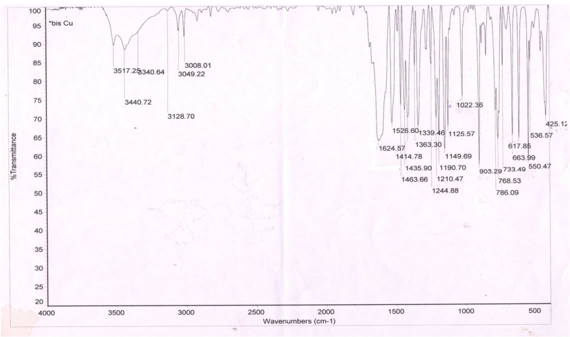


Figure - 4: FT-IR Spectra of Cu(II) complex using KBr pellets.

3.4. ^{1}H-NMR and ^{13}C-NMR spectra

The mannich base ligand has symmetry element in it and so spectrum of half of the molecule similar to another half. The ^{1}H-NMR spectrum of the ligand showed the following resonance signals: Signals due to aromatic protons appear at 6.94-7.00 and 7.41-7.53 δppm as two multiplets, N-H proton chemical shift occurs at 8.050-8.055 as weak doublet. The piperazine protons signals occur at 3.63-3.68 δppm. The methyl group protons exhibit an intense signal at 2.00 δppm. The methine proton signal appears at 5.87-5.89 δppm as weak boublet. The peak at 9.85 δppm is attributed to the phenolic –OH group present in salicylaldehyde. The presence of phenolic OH protons peak in Zn (II) complex confirmed that the –OH proton is free from complexation, the doublet of N-H proton shifted down field 8.01ppm and N-CH_2 proton also shifted 3.55ppm further confirmed the nitrogen from piperazine and oxygen from amide involved in coordination with central metal ion. The ^{13}C-NMR spectrum of the ligand showed the following signal at 173.35(C=O), 161.62(C-OH), 137.08, 133.30, 120.73, 119.94, 117.62 (Ar-Carbons), 69.70(CH), 58.23(N-CH_2), 22.57(CH_3) well supported for our expected structure.

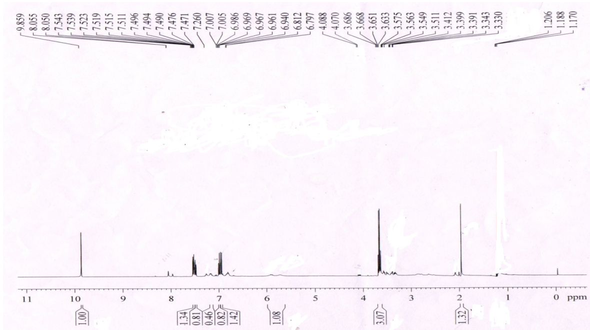


Figure - 2: ^{1}H-NMR Spectra of ligand in $CDCl_3$ solvent.

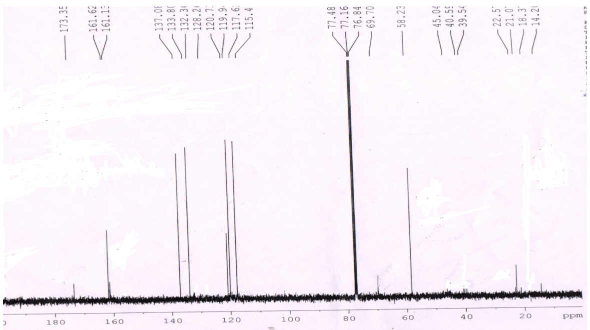


Figure - 3: ^{13}C-NMR spectra of ligand in $CDCl_3$ solvent.

Table-1: Analytical and physical data of ligand and complexes

Compounds	Yield (%)	Mp (^{o}C)	Colour	*μeff* (BM)	M. conductance ($\Omega^{-1}cm^{2}mol^{-1}$in 10^{-3})
BMB-L	65	160-165	Light yellow	----	-----
BMB-Cu	54	<300	Dark green	1.8	1.72
BMB-Ni	45	<300	Light green	2.7	2.00
BMB-Co	35	<300	orange	3.8	2.37
BMB-Zn	50	<300	white	Diamagnetic	1.9

Table - 2: IR-Spectral data of ligand and their complexes

Compounds	Vibration frequency of various functional groups (in cm^{-1})					
	-OH	-NH	C=O	CNC	M-O	M-N
BMB-L	3454	3228	1655	1292	-------	------
BMB-Cu	3440	3340	1624	1210	550	425
BMB-Ni	3443	3193	1604	1195	533	438
BMB-Co	3432	3300	1604	1197	583	495
BMB-Zn	3462	3270	1624	1150	560	452

Table -3: Antibacterial activity of ligand and complexes

Bacteria	Standard Antibiotic Disk(streptomycin)	Zone of inhibition mm in diameter (10µg/disc)				
		BMB - L	BMB - Cu	BMB - Ni	BMB - Co	BMB - Zn
Staphylococcus aureus	18	07	15	10	07	12
Staphylococcus epidermidis	17	16	12	09	08	28
Escherichia coli	24	07	18	14	-	11
Pseudomonas aeruginosa	25	06	12	15	07	8

Table - 4: Antifungal activity activity of ligand and complexes

Fungi	Standard Antibiotic Disk (Amphotericin-B)	Zone of inhibition mm in diameter (10µg/disc)				
		BMB - L	BMB - Cu	BMB - Ni	BMB - Co	BMB - Zn
Aspergillus niger	12	-	-	8	-	09
Candida albicans	08	19	28	22	10	20

3. 4. Antimicrobial and antifungal activity

The antibacterial activities of both ligand (L) and its metal complexes were studied by usual agar disc diffusion method. The bacterial species used in the screening were staphylococcus aureus, staphylococcus epidermidis (gram positive) Escherichia coli, Pseudomonas aeruginosa (gram negative) and fungus were aspergillus niger, candida albicans. Stock cultures of the test bacterias and fungi species were maintained on Nutrient Agar media by sub culturing on petri dishes. The media were prepared by adding the components as per manufacturer's instructions and sterilized in the autoclave at 121°C temperature and 15lbs pressure for 15 minutes and then cooled to 45-60°C. The 20mL of each medium was poured in a Petri dish and allowed to solidify and after solidification, Petri plates with media were spread with 1.0 mL of bacterial suspension, which is prepared in sterile distilled water. The wells were bored with cork borer and the agar plugs were removed. 100 µl of the compound reconstituted in DMF (Dimethyl formamide) in concentrations of 1.0 mg/mL was added to the agar wells.The plates were incubated at 37°C for 24 hours and then the plates were observed for the growth inhibition zones. The presence of clear zones around the wells indicated that the compound is active. The diameter of the zone of inhibition was calculated in millimeters. The well diameter was deducted from the zone diameter to get the actual zone of the inhibition diameter and the values have been tabulated. Results of bactericidal screening showed that the chelation tends to make the ligand act as more powerful and potent bactericidal agents, thus killing more of the bacteria than the free ligand. The metal complexes showed excellent antifungal activity against Candida albicans but there is no significant activity against aspergillus niger except Ni(II) and Zn(II) complexes.

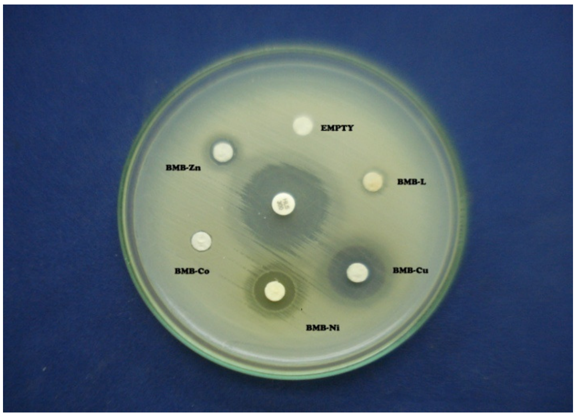


Figure - 6: Antibacterial activity staphylococcus aureus

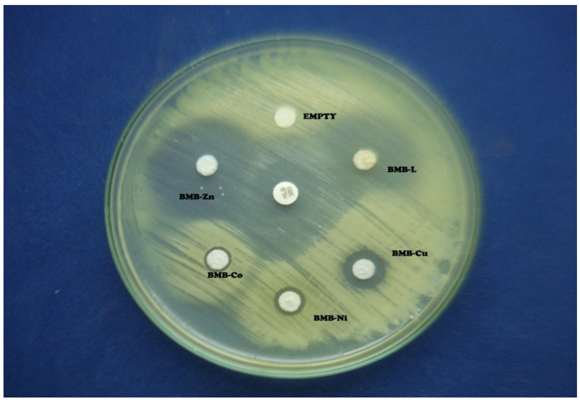


Figure - 6: Antibacterial activity staphylococcus epidermidis

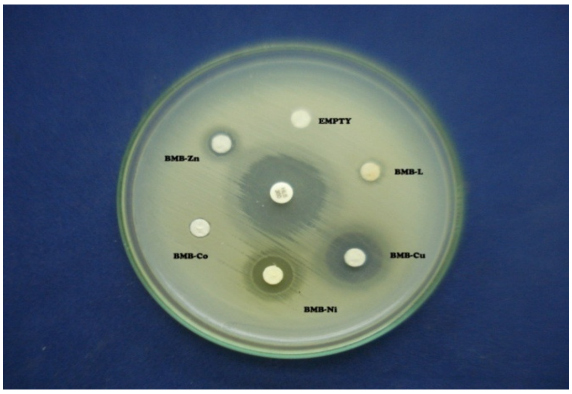


Figure - 6: Antibacterial activity Pseudomonas aeruginosa

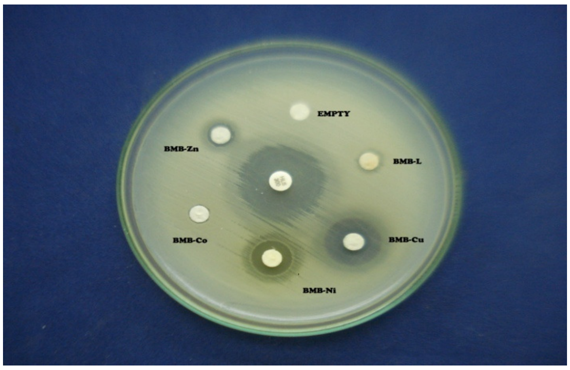


Figure - 6: Antibacterial activity Escherichia coli

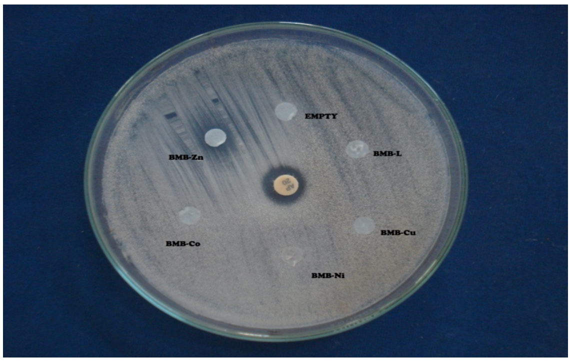


Figure -7: Antifungal activity Aspergillus niger

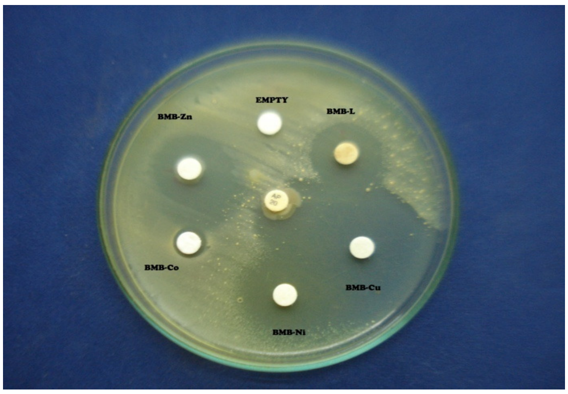


Figure -7: Antifungal activity Candida albicans

4. CONCLUSION

It may be concluded that the ligand behaves as bidentate chelating agent and the spectroscopic techniques well supported to our proposed structure. Metal complexes showed potent microbial activity than the ligand was observed which was explained on the basis of chelation theory. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive 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.

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