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Exploration of transition metal complexes (Co, Cu and Zn) and their antimicrobial activity with a new Mannich base of N-[(2-hydroxy-phenyl)-phenylamino-methyl]-benzamide (SAB)

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Abstract— Mannich condensation yields Mannich bases which could display more potent pharmacological properties like antipsychotic, anticonvulsant, anthelmintic, antibacterial, antimalarial activities. The ligand was synthesized by Mannich condensation reaction between salicylaldehyde, aniline and benzamide. The present work deals with the structure of some metal complexes of Co(II), Cu(II) and Zn(II) with a new Mannish base N-[(2-hydroxy-phenyl)-phenylamino-methyl]-benzamide (SAB). The ligand and the complexes have been characterized by various physico-chemical techniques such as elemental analysis, molar conductance, magnetic susceptibility, FT-IR, UV-Vis., ^{1}H & ^{13}C NMR and TGA/DTA. Antimicrobial activities of the ligand and its complexes were tested against gram positive S.aureus and gram negative E.Coli bacteria and antifungal activity against A.niger.

Index Terms— Antimicrobial activities, ^{1}H & ^{13}C NMR, Metal complexes, N-[(2-hydroxy-phenyl)-phenylamino-methyl]-benzamide (SAB) and Thermal analysis,

1 Introduction

THE benzamide contain a phenyl ring fused to a ring. Benzamide and their derivatives have diverse applications in coordination chemistry, photo chemistry and bio-inorganic chemistry [1-4]. Many of the Mannich base compounds synthesized by the condensation of aldehyde, amine and amide have been recorded. The synthetic compounds have widespread pharmaceutical importance of (i.e) antibacterial, antifungal, anti-inflammatory [5-7] and analgesic [8] properties. In addition to their biological importance, the compound form stable complexes with various transition metals [9]. The main objective of present communication is to provide a comprehensive amount of Mannich base, their chelating behavior and to highlight their potential in evolving better antimicrobial drugs. A Mannich base and transition metal (II) complexes have been prepared in this study and well characterized by their physical, spectral and analytical data. The synthesized compounds were further evaluated for their antimicrobial properties against various pathogens using disc method.

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2 Experimental Methods

2.1 Materials and Methods

Reagents such as salicylaldehyde, aniline, benzamide were of Merck products and were used as such. The melting points of all compounds were determined in open capillaries and uncorrected [10-11]. The elemental analysis of C,H,N were carried out at the elemental analyzer namely elemental model ratio EL(III), CECRI-Karaikudi. FT-IR spectra were measured using KBr pellets with Perkin Elmer RX_1 spectrophotometer in the conventional range of 4000-400 cm^{-1}. ^{1}H & ^{13}C NMR spectra of the free ligand and its Zinc (II) complex in DMSO-d_6 were recorded in a BRUKER, Switzerland Avance 400 MHz NMR spectrometer using tetra methyl silane as internal standard. Their antimicrobial properties were studied against various pathogens using disc diffusion method.

2.2 Synthesis of Ligand (L)

The ligand was synthesized by 0.01M of benzamide in 20 ml of ethanol, 0.01M of salicylaldehyde and 0.01M primary amine like aniline were added. After the constant stirring of mixture for an hour, an yellow colour solid mass was obtained and this compound was recrystalized from ethanol. The compound was kept in hot air oven at 60°C. It melts at 90°C [12].

2.3 Synthesis of Metal Complexes

Hot ethanolic solutions of corresponding metal chlorides were slowly mixed with hot ethanolic solution of the respective ligand (1:1 mole ratio) with constant stirring. The mixture was refluxed for 5-6 hours between 70-80°C and cooled the con-

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tents. The colored complexes were separated out in all the complexes. It was filtered and washed with ethanol and dried at vacuum desiccators (yield: 75-80%).

3 Results and Discussion

3.1 Fourier Transform Infra-Red Spectroscopy

The FT-IR spectra of the Mannich base ligand (SAB) and its complexes are studied. They are presented in TABLE 1. The 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 SAB, the infra-red bands observed at 3367, 1625 and 1195cm^{-1} have been assigned to υ_{N-H}, $\upsilon_{C=O}$ and υ_{C-N-C} respectively. In this spectra of all the complexes, the υ_{N-H} band remains at the same or high position as in the free ligand, indicating that the amide nitrogen is not coordinated. A band due to υ_{C-N-C} stretching vibration of the aniline ring appeared at 1195 cm^{-1} in the Mannich base. This band is shifted to 1180-1190 cm^{-1} in the metal complexes, suggesting the involvement of the nitrogen atom from the aniline ring to the central metal ion. The oxygen atom present in amide to be involved in the coordination to the metal ion. The new bands 750-760, 685-700 and 500-540 cm^{-1} in the spectra of the metal complexes were assigned to υ_{M-O}, υ_{M-N} and υ_{M-X} stretching vibrations respectively [13-15]. The presence of coordinated water molecules in Cu(II) complex is determined by the appearance of bands at 3350-3400 cm^{-1} and the peak at 800-850cm^{-1} assignable to the O-H stretching and rocking made of coordinated water molecules.

TABLE 1
FT-IR SPECTRAL DATA FOR SAB(L) AND METAL COMPLEXES

Compound	$\nu_{C=O}$	ν_{N-H}	ν_{C-N-C}	ν_{M-O}	ν_{M-N}	ν_{M-X}
SAB-L	1625	3367	1195	-	-	-
SAB.$CoCl_2$.H_2O	1619	3369	1179	758	686	506
SAB.$CuCl_2$.H_2O	1600	3390	1184	757	699	535
SAB.$ZnCl_2$.H_2O	1613	3361	1180	757	691	528

3.2 Electronic Spectra and Magnetic Moments

The electronic spectra of Co(II) complex exhibits one band at 27,000-28000 which may reasonably be assignable to $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transition. The magnetic moments for Co(II) complexes 4.6-4.8 BM are within the range of an octahedral geometry [16]. The observed magnetic moments for Cu(II) complex exhibits two bands at 17500-19000, 26500-27500 which may assignable to $^2B_{1g} \rightarrow {}^2Eg$ and CT transitions. The magnetic moments for Cu(II) complexes1.7-1.8 BM are within the range of an octahedral geometry [17-18].

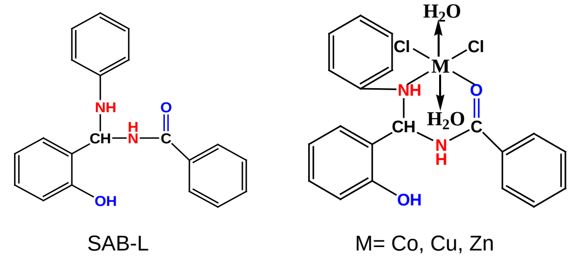

Fig 2. Structures of Mannich base SAB (L) and metal complexes

3.3 Thermal Analysis

The Co(II) complex is stable up to 140°C. An endothermic peak observed at ~140°C shows the loss of coordinated H_2O to give the anhydrous complex. Decomposition of the anhydrous complex occurs in the temperature range 140-450°C to form an intermediate of $CoCl_2$. When heated above 450°C the decomposition of $CoCl_2$ is decomposed to the final residue of CoO. The same is indicated by an exothermic at 520°C.

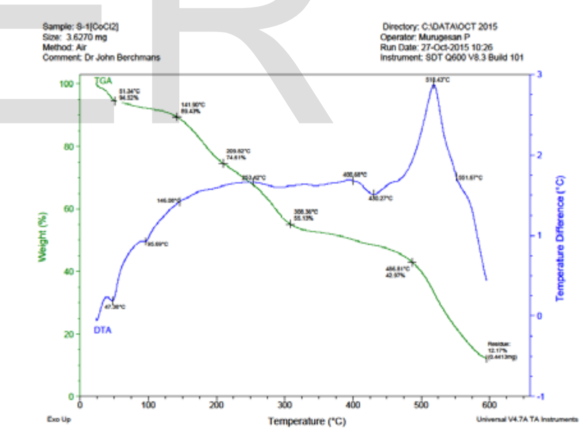

Fig. 2. TGA/DTA Spectrum of SAB.$CoCl_2$.H_2O

3.4 NMR Spectral Data of Ligand (L)

^{1}H NMR (DMSO-d$_6$, δppm): 9 (OH), 2-3 (Ali-CH), 6-7 (N-H), 6.9-8.0 (Aro-CH proton)

^{13}C NMR (DMSO-d$_6$, δppm): 170-180 (carbonyl carbon), 115-140 (Aro-carbon), 50-60 (Ali-CH carbon)

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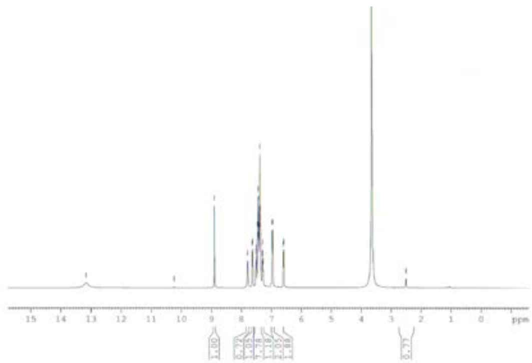

Fig. 3. ^{1}H NMR Spectrum of SAB

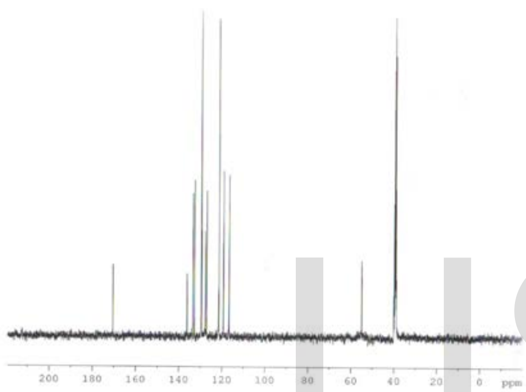

Fig. 4. ^{13}C NMR Spectrum of SAB

4 ANTIMICROBIAL STUDY

4.1 Antibacterial Activities of SAB and its Metal Complexes

About two organisms were utilized to detect the antibiotic activity of the complexes in tested bacterial strains. The sensitivity of a microorganism to antibiotics and other antimicrobial agents were determined by the assay plates which were incubated at 37±2 °C for about 2 days. As a result in this study, the metal chloro complexes have high inhibition efficiency than the ligand against the bacterial species.

The variation in the biological activity was due to the nature of the metal ions and also the cell membrane of the microorganisms. Due to the decrease in the charge localization of the metal ion that leads to more lipid solubility, the metal chloro complexes have higher bioactivity than that of the SAB-ligand. The potential of the complex is, on complexation the polarity of ion reduces 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.

The antibacterial activity of the complexes were determined by disc diffusion method and compared with the metal complexes. Streptomycin is used as standard.

The result shows that the metal complexes have good activity compared to than that of the free SAB. This fact confirms from the tweedy chelation theory.

Thus, the order of activity of the metal chloro complexes

TABLE 2
ANTIBACTERIAL ACTIVITIES OF SAB AND METAL COMPLEXES

Compound	Zone of Inhibition (mm)	
	E.Coli (-)	S.aureus (+)
SAB-L	4	5
SAB.$CoCl_2.H_2O$	11	10
SAB.$CuCl_2.H_2O$	8	9
SAB.$ZnCl_2.H_2O$	5	6
Streptomycin – Std.	9	7
DMF – solvent control	2	1

Concentration of the compound= 25µg/mL

of SAB against gram negative bacterium E.Coli is,

SAB.$CoCl_2$>SAB.$CuCl_2.H_2O$>SAB.$ZnCl_2.H_2O$>SAB.L

Co^{II}, Cu^{II} complexes are highly active against E.Coli and Zn^{II} complex is moderately active.

The order of activity of the metal chloro complexes of SAB against gram positive bacterium S.aureus is,

SAB.$CoCl_2$>SAB.$CuCl_2.H_2O$>SAB.$ZnCl_2.H_2O$>SAB.L

Cu^{II}, Co^{II} complexes are highly active against S.aureus Zn^{II} complex is moderately active.

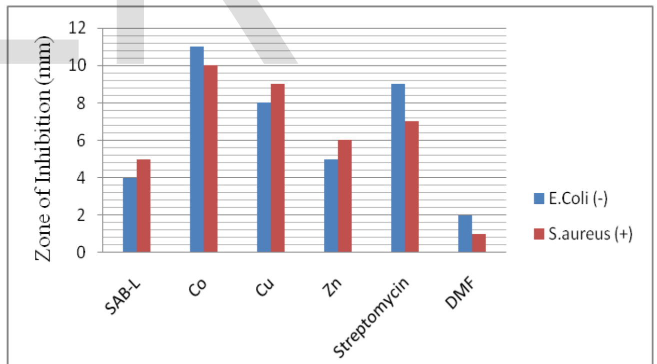

Fig.5 Correlation Diagram of Antibacterial Activities

4.2 Antifungal Activities of SAB and its Metal Complexes

Like, antibacterial activity, the resistivity of the metal chloro complexes were evaluated at 25µg/mL concentration by paper disc diffusion method. Papastin was used as standard and DMF as solvent control.

The antifungal activity of the metal chloro complexes were tested against A.niger. As a result, the metal complexes have good resistivity compared to than that of free SAB.

The order of resistivity of the metal chloro complexes against the fungal species A.niger is,

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$SAB.CuCl_2.H_2O > SAB.CoCl_2 \approx SAB.ZnCl_2.H_2O > SAB.L$

TABLE 3

ANTIFUNGAL ACTIVITIES OF SAB AND METAL COMPLEXES

Compound	Zone of Inhibition (mm)
	A.niger
SAB-L	6
$SAB.CoCl_2.H_2O$	7
$SAB.CuCl_2.H_2O$	8
$SAB.ZnCl_2.H_2O$	7
Papastin – Std.	11
DMF – Solvent Control	1

Concentration of the compound= 25µg/mL

Cu^{II} chloro complex is highly resistive against A.niger fungal species. Co^{II}, Zn^{II} chloro complexes are moderately resistive against A.niger.

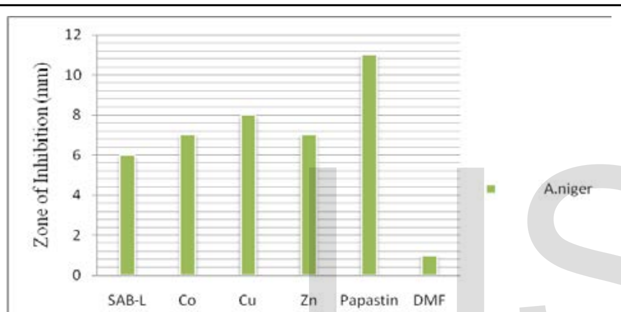

Fig.6 Correlation Diagram of Antifungal Activities

4 CONCLUSION

The new Mannich base N-[(2-Hydroxy-phenyl)-phenylamino-methyl]-benzamide (SAB) and Co(II), Cu(II) and Zn(II) metal complexes were synthesized and characterized. The structural analysis data established on the basis of elemental analysis (C,H,N), FTIR, UV, ^{1}H and ^{13}C NMR, magnetic susceptibility and TGA/DTA patterns of complexes were recorded and discussed. The antimicrobial activity of the various substituted SAB compounds has been extensively studied on microorganisms such as S.aureus, E.coli and A.niger by disc diffusion method. It has been found they exhibit good inhibition property.

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REFERENCES

[1] X. C. Huang, J. P. Zhang, X.M. Chen., A New Route to Supramolecular Isomers via Molecular Templating: Nanosized Molecular Polygons of Copper(I) 2-Methylimidazolates, J. Am. Chem. Soc., 126 (41), 2004, 13218-13219.

[2] T. J. Cardwell, A. J. Edwards, R. M. Hartshorn, R. J. Holmes., Structural and Electrochemical Studies of Some Cobalt(III) Complexes of 2-Aminomethylbenzimidazole and 2-(N-Methylaminomethyl) benzimidazole, Aust. J. Chem., 50(10), 1997, 1009-1015.

[3] Y. P. Tong, S. L. Zheng., Synthesis, structure, spectroscopic properties, DFT and TDDFT investigations of copper(II) complex with 2-(2-hydroxyphenyl)benzimidazole, J. Mol. Struct., 841(1-3), 2007, 34-40.

[4] Y. P. Tong, S. L. Zheng, X. M. Chen, Experimental and theoretical studies on the electronic structure of trisubstituted boroxine,J. Mol. Struct., 841 (1-3), 2007, 104-112.

[5] S. Murugesan, S. Sathiyamoorthy., J. Pharm. Res., 44(5), 2011, 222-226.

[6] V. Kamlesh, S. Patel, Eur. J. Chem., 15 (5-6), 2009, 281-288.

[7] B.A. Reddy, Eur. J. Chem., 7, 2010, 222-226.

[8] E.P. Jesudason, S.K. Sridhar, E.J. Padma, et al., Synthesis, pharmacological screening, quantum chemical and *in vitro*permeability studies of *N*-Mannich bases of benzimidazoles through bovine cornea, Eur. J. Med. Chem., 44(5), 2009, 2307-2312.

[9] K.C. Rout, R.R. Mohanty, S. Jena, K.C. Dash., S. Jena, K.C. Dash., Dioxouranium(VI) and thorium(IV) complexes with 2(2′ -pyridyl)1-methylbenzimidazole and reaction of dioxouranium(VI) complex with mercury(II), cobalt(II) and nickel(II) PolyhedronPolyhedron, 15(5-6), 1996, 1023 -1029.

[10] S.N. Pandeya, Ranjana, synthesis and antimicrobial activity of ciprofloxacin schiff and mannich base, Int.J.Chem.Tech Res., 4, 2012, 778-785.

[11] M. Shanmuapriya, A. Abdul Jameel, M. Syed Ali Padusha., Synthesis, characterization and antimicrobial activities of salicylaldehyde derivatives, Int.J.PharmTech Res., 4(1), 2012, 85-88.

[12] L. Muruganatham, K. Balasubramaniyan., J.Chem.Bio.Phy.Sci. 3, 2012, 1184-1191.

[13] Lever ABP., Elsevier, New York, 1968.

[14] K.K. Narang, A. Agarwal, , Salicylaldehyde salicylhydrazone complexes of some transition metal ions, Inorg Chim Acta., 9(L2), 1974, 137-142.

[15] Lever ABP, Mantovani, Far-infrared and electronic spectra of some bis(ethylenediamine) and related complexes of copper(II) and the relevance of these data to tetragonal distortion and bond strengths, E. Inorgchem,10(4), 1971, 817-826.

[16] R.K. Agarwal, P. Garg, H. Agarwal., Synthesis, Magneto-Spectral and Thermal Studies of Cobalt(II) and Nickel(II) Complexes of 4-[N-(4-Dimethylaminobenzylidene) amino] Antipyrine, Synth. React.Inorg. Met-Org. Chem., 27(2), 1997, 251-268.

[17] S. Murugesan, S. Sathiyamoorthy., J.Pharm.Res. 4, 2011, 2679-2681

[18] P.K Panchal, M.N. Patel., Strructural Characterization and Antibacterial Studies of Some Mixed – Ligand First Row d- Transition Metal Complexes, Synth.React.Inorg.Met.-Org.Chem., 34(7), 2004,1277-1289.