Original Research Article

Schiff bases and their medical importance

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Abstract

Schiff base ligands and their metal complexes are very important in medicinal and pharmaceutical fields because of their wide spectrum of biological activities. Schiff bases are the compounds which are mainly formed by the condensation reaction between carbonyl compounds and amines. These compounds can be synthesized by various synthetic routes. Some of those are easily synthesized from the various heterocyclic rings like furan, pyridine, thiophene and the most important triazoles especially 1,2,4-Triazole. The chemistry of Triazole compounds has expected considerable interest due to their synthetic and effective biological properties. This research work involves the preparation of biologically active metal complexes of Ni(II), Mn(II) Chlorides with the Schiff base ligand derived from 4-amino-1,2,4-Triazole and 2-hydroxybenzaldehyde. The prepared ligand and its metal complexes were evaluated for antibacterial activities.
Key Words: Coordination chemistry, Schiff bases, metal complexes, biological activity.

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Quick Response Code:

Website: www.medpulse.in

Accessed Date: 26 March 2018

INTRODUCTION

Schiff bases are the compounds derived from an amine and carbonyl compounds which in coordination with metal ions through the azomethine nitrogen (HC=N) form good chelating agents.[1] Schiff bases containing various donor sites have been tried for complexation and the structures were deduced with the help of spectral and magnetic data.[2,3] Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable.[4] Schiff bases are generally bidentate,[5-6] tridentate,[7] tetradentate[8] or polydentate[9] ligands competent of forming stable complexes with transition metals.[10] Schiff base metal complexes had been a widely studied subject due to their industrial and biological applications.[11] A large number of Schiff bases have potential biological interest, being used as more or less successful models of biological compounds. They played a key role in the development of modern chemistry, but they can also be found at key points in the development of inorganic biochemistry, catalysis, optical materials and other fields. Antibacterial activities of Schiff bases like nitro and phenyl derivatives are more active[12]. Triazole ligands and their metal complexes are very important in medicinal and pharmaceutical sciences because of their wide spectrum of biological activities[13]. The present paper deals with the synthesis and biological investigation of 4-amino-1,2,4-triazole-salicylaldimine Schiff base derived from 4-amino-1,2,4-triazole and salicylaldehyde and its Ni(II) and Mn(II) complexes.

MATERIALS AND METHODS

Chemicals: All the chemicals used were of GR/AR grade. A pure sample of 4-Amino-1,2,4-triazole, molecular formula $C_2H_4N_4$ was obtained from Loba Chem. Ltd. The metal salt of $NiCl_2$ and $MnCl_2$ were from Hi-media Pharmaceuticals Ltd. Solvents used were ethanol, acetone, and DMF.

Synthesis of Ligand: A mixture of 4-amino-1,2,4-triazole(0.1 mol) with salicylaldehyde (0.1 mol) in 30 ml of ethanol was refluxed for about 3 hours with the addition of few drops of Sulphuric acid with occassional shaking of the solution. The product, which was separated out as a crystalline solid on cooling, filtered and recrystallized from the ethanol.

Synthesis of Metal Complexes: Mixing of selected metal salts of $NiCl_2$ and $MnCl_2$ (0.01M) in 30 ml of ethanol with 30 ml solution of Schiff base (0.02 M) was carried

out separately with constant stirring. The resulting mixture was refluxed for about 2 hours with occasional shaking until precipitation occurs. After precipitation, the resulting complexes were collected by filtration, washed with the same solvent and recrystallized with acetone.

Physical Measurements: Elemental analysis was performed on Perkin Elmer 240C Model Elemental Analyzer at IIT Powai, Mumbai. The melting points of the ligand and the complexes were determined in open capillaries with electronic melting point apparatus and are uncorrected. The infra-red spectra of Schiff base and derived complexes were recorded with FT-IR spectrophotometer Model RZX (Perkin Elmer) using KBr pellets in the range of 4000cm^{-1} - 400 cm^{-1} at SAIF, Panjab University Chandigarh. Electronic spectra were also recorded on a UV-VIS-Spectrophotometer Model Synthesis Lambda 750 Perkin Elmer at SAIF, Panjab University, Chandigarh.

Biological Activity: Schiff bases and its derived metal complexes were tested against two Gram-positive and two Gram-negative bacterial strains. The in-vitro antibacterial activity of the Schiff base and its derived metal complexes was determined by Disc diffusion method[14] against bacterial strains. The test organisms were grown on Nutrient Agar medium in Petri plates and then agar plates were left to solidify at room temperature. After solidification, the disc of Whatman filter paper with 20µL of prepared Schiff base and metal complex solutions was carefully placed with the help of forceps at the center of the Petri dish and then kept at 37±0.1^{o}C for 24 hours in an incubator. The zone of inhibition was measured.

RESULTS AND DISCUSSION

The Schiff base ligand and its complexes are subjected to elemental analyses. The results of elemental analyses (C, H, N, S) with molecular formula are presented in Table 1. The analytical data for the complexes suggested 1:2 stoichiometry for the entire synthesized complex.

Table 1: Elemental analysis of Schiff base and its derived metal complex

Ligand /Complex	Mol. Wt	Color	M.P (^{o}C)	Elemental Analysis Found (Calcd.) (%)			
				C	H	N	M
At-S $C_9H_8N_4O$	188.18	White	170	58.19 (57.90)	4.00 (4.18)	31.90 (28.9)	-
$[Ni(At\text{-}S)_2].2H_2O$ $C_{18}H_{18}N_8O_4Ni$	469.08	Bluish Green	280	45.91 (46.07)	3.00 (2.47)	19.10 (19.55)	19.95 (18.60)
$[Mn(At\text{-}S)_2].2H_2O$ $C_{18}H_{18}N_8O_4Mn$	465.32	Light Green	>300	43.9 (44.05)	3.60 (3.9)	25.00 (24.09)	12.06 (11.90)

IR Spectral Studies: The comperative interpretation of Schiff base and derived metal complexes were shown in table 2. The IR spectra of complexes indicates that the Schiff base (ligand) acts as a tridentate ligand, using phenolic oxygen[15] and azomethine nitrogen and nitrogen of triazole ring as donor atoms. The ligand shows the strong band at 3425 cm^{-1} due to phenolic –OH group. This band is absent in the respective metal complexes indicating the involvement of this group in complex formation.[16-17] The IR spectrum of the Schiff base shows a strong band at 1609 cm^{-1} attributed to $\nu_{(HC=N)}$ stretching vibrations of the azomethine group, which gets shifted to higher frequency regions 1628 cm^{-1} and 1645 cm^{-1} in the complexes representing involvement of the nitrogen atom of azomethine group.[18-20] The band at 1569 cm^{-1} is due to the $\nu_{(C=N)}$ stretching and this frequency shifted to a lower frequency value of 1535 cm^{-1} and 1543 cm^{-1} in the complexes confirming the involvement of the (C=N) in the coordination with the metal ions2[1]. The stretching vibrational band C-O of the ligand lies at 1373 cm^{-1} frequency.[22-23] This band shifts to 1420 cm^{-1} higher frequency side in the complex of Ni(II) and 1246 cm^{-1} a lower frequency side in the complex of Mn(II).

Table 2: Important IR Spectral band values (cm^{-1}) of ligand and complexes

Ligand/ Complex	$\upsilon_{(HC=N)}$	υ_{C-O}	$\upsilon_{C=N}$	υ_{OH}	Chelate ring
At-S $C_9H_8N_4O$	1609s	1373s	1569s	3425s	1425s
$[Ni(At\text{-}S)_2].2H_2O$ $C_{18}H_{18}N_8O_4Ni$	1628s	1420s	1535s	-	1408s
$[Mn(At\text{-})_2].2H_2O$ $C_{18}H_{18}N_8O_4Mn$	1645s	1246s	1543s	-	1445s

Electronic Spectral Studies: The solid reflectance spectrum of Ni (II) complex is consistent with the formation of an octahedral geometry with the appearance of three bands at 22728, 18518 and 10472 cm^{-1} corresponding to the transitions $^3A_2g \rightarrow {}^3T_1g(P)$, $^3A_2g \rightarrow {}^3T_1g(F)$ and $^3A_2g \rightarrow {}^3T_2g(F)$ [24-25]. The electronic spectrum of Mn(II) complex shows three band positions at 26741, 20745 and 19811cm^{-1} which are assigned to $^6A_1g \rightarrow {}^6T_1g(G)$, $^6A_1g \rightarrow {}^4T_2g(G)$, and $^6A_1g \rightarrow {}^4T_1g(G)$

transitions, respectively indicating octahedral geometry[26]. **Biological Activity:** Schiff bases and its derived metal complexes were tested against two Gram-positive *S. aureus* ,*B. subtilis* and two Gram-negative *E. coli*, *P. aeruginosa* bacterial strains. *The in-vitro* antibacterial activity of the Schiff base and its derived metal complexes was determined by Disc diffusion method[14] against bacterial strains. The *in vitro* antibacterial investigation results are given in Table-3. It has been observed that all compounds exhibited very significant and better antibacterial activity. The free ligand (Schiff base) shows potent activity against *E. coli* bacterial strain with inhibition of 13 mm. Among the metal complexes Ni(II) complex show higher antibacterial activity in case of *S. aureus* and *E. coli* with zone of inhibition of 14 mm. The Mn(II) complex show moderate activity in case of *P. aeruginosa* with zone of inhibition of 15 mm. These observations show that both of the metal complexes are more active than the free ligand.

Table 3: Antibacterial activity of Schiff base (AT-S) and its derived metal complexes

Compound	*S. aureus*	*B. subtilis*	*E. coli*	*P. aeroginosa*
AT-S	12±0.41	11±0.22	13±0.34	12±0.44
AT-S-Ni	14±0.23	13±0.45	14±0.51	12±0.23
AT-S-Mn	13±0.36	14±0.35	13±0.41	15±0.48
TETRACYCLINE	17±0.37	15±0.32	17±0.48	16±0.35

CONCLUSION

The Schiff base ligand (AT-S) acts as a neutral tridentate ligand coordinating through the oxygen of the phenolic group, the nitrogen of the azomethine group and triazole nitrogen. On the basis of analytical and spectral studies octahedral geometry is proposed to Ni (II) and Mn(II) complexes. Both metal complexes show enhanced biological activities than Schiff base ligand.

ACKNOWLEDGEMENT

The authors are thankful to Principal, Sadhu Vaswani College, Bairagarh for providing necessary facilities for research work and DST for granting FIST program to the college.

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Source of Support: None Declared
Conflict of Interest: None Declared