Journal of Advances and Scholarly Researches in Allied Education
Vol. 20, Issue No. 1, January-2023, ISSN 2230-7540

Antibacterial and Antifungal studies on Schiff Base Complexes by the Minimum Inhibitory Concentration (MIC) method

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Abstract - The aim of the present study is to study the antibacterial and antifungal activities of the binuclear Schiff Base complexes of Ni (II) and Cu(II) metal salts. The plan of the research work was to analysed the molar inhibitory concentration (MIC) in molar concentration (*10*) of FAHMC (Furan-2-aldehyde 8-amino-7-hydroxy-4-methyl coumarin) and its Metal Ni(II) and Cu (II) complexes. The results were found that molar inhibitory concentration the Furan-2-aldehyde 8-amino-7-hydroxy-4-methyl coumarin FAHMC= Furan-2-aldehyde-8-amino-7-hydroxy-4- methyl coumarin. [Cu (FAHMC)$_2$] =Furan-2-aldehyde-8-amino-7-hydroxy-4- methyl coumarin. Cu(II) and [Ni (FAHMC)$_2$ (H2O)$_2$] = Aqua furan-2-aldehyde-8-amino-7-hydroxy-4-methyl Ni(II). The results support hypothesis.

Keywords - Schiff-base complexes, FAHMC, Antibacterial, antifungal, MIC, Staphylococcus aureus, Escherichia coli

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INTRODUCTION

Metal complexes of Schiff bases have occupied a central role in the development of coordination chemistry. Schiff bases diformyl precursors with the primary mono-amine derivatives we can derive the [1+2] symmetric end-off Schiff base ligands as shown Figure 28a where the reaction of these Schiff bases consisting of two identical adjacent coordination chambers. The corresponding homodinuclear complexes are obtained with *d*-metal ions in a molar ratio of 1:2 (ligand to metal ratio) and with symmetric end-off Schiff base ligands and in the presence of base as deprotonating agent, although the mononuclear complexation could be also achieved by occupying a 1:1 (ligand to metal) molar ratio. The both mono-nuclear and di- nuclear complexation could be achieved in the presence of a template. The compounds containing the azomethine group (-RC=N-). These are characterized by the structure RR'c-NR" (where RR'C represents an aldehyde or a ketone residue and =NR" is the amino residue of a primary amine). These compounds are also termed as amines, azomethines or anils. The Schiff bases are effective as coordinating ligands having active functional groups like, -OH, -SH, -COOH etc. in ortho position to >C=N- group. These form stable chelates. The Schiff bases may act as bi-, tri-, tetra-, penta-, hexa-, or polydentate chelating agents depending upon the number of available functional groups present in the right position. Similarly in order to prevent the polymerize action the different polyamine derivatives could be used for the synthesis of [1+2] acyclic Schiff base ligands in the presence of a template. In the formation of the appropriate metal salts and base, these polyamine derivatives ligands normally result in homonuclear complexes as well. The resulting mono- or di-nuclear complexes contains endogenous donor atoms, such as pyridine, N; pyridazine N, N; phenolate -O- or a thiophenolate sulfur -S-. Several reports on the synthesis and characterization of binuclear transition metal complexes with 'end-off' compartmental Schiff bases has emerged out where these complexes have been prepared by stepwise procedures or template, where bridging phenolate oxygen with the other bridging groups like Cl, Br, OH, 1,1-N_3 , 1,3-N_3 or 1-OCN could be involved. These complexes have potential relevance as enzyme models as a frequently modeled protein centre is that of the binuclear copper(II) active site in the oxygen transport protein haemocyanin.

MIC- The graded dilutions of the test compounds in a suitable nutrient medium are inoculated with organism under examination using aseptic techniques and incubated under suitable conditions in an incubator. The minimum concentration of the compound preventing detectable growth (MIC) is taken as a measure of biocidal activity. Further we observed that the taste of organisms like: - Bacteria it is Staphylococcus aureus (Gram positive) and Escherichia coli (Gram negative). Another one is Fungi- Aspergillus niger, Aspergillus nidulense and Candida albicans.

Subculture of the above-mentioned microorganisms were prepared monthly from the principle culture and broth culture weekly from the subculture. All cultures were stored at 4°C. The inoculation process was carried out in a well cleaned inoculation chamber having UV lamp. Seeded broth for the test to be conducted was prepared by diluting the broth culture of the desired organism in 1:100 times and already kept for overnight at their optimum temperature. Several metal ions have been studied gravemetrically and spectrophotometrically using acetyl, hydroxy coumarin, Phenyldaphnetin and benzy, dihydroxy coumarin. Spectral and magnetic properties of uranyl (VI) complexes involving, hydroxy, methyl, coumarin, carboxylic acid was involving, hydroxy, methyl, coumarin, carboxylic acid was studied by Rastogi. Rastogi et al. also studied the complexes of Ni (II) and Cu (II) with amino, hdroxy, methyl coumarin, p-chloroaniline and acetyl acetone derived Schiff bases uranyl (VI) complexes were prepared by Kulkarni et MADA et., al. complex, one Zn(II) ion was of five-coordinated geometry which was intermediate between trigonal-bipyramid and square-pyramid with further coordination of one pyridine molecule. Whereas a six-coordinate octahedral geometry with two coordinated pyridine molecules was detected for the other Zn(II) ion. But it was reported to have same geometries for the both Ni(II) ions in the complex, which was six-coordinated octahedral geometry with two pyridine molecules at *axial* sites in each Ni(II) ions. Ni(II) complex reported to have antiferromagnetic interaction operation between the two Ni(II) ions, while Zn(II) complex was diamagnetic in nature. Experiment recorded magnetic moment of $[Ni_2(L)(OH)(py)_4](ClO_4)_2]$ at room temperature to be 2.92 B.M. which was again reported to be decrease to 0.28 B.M. with temperature falling down to 2K which indicates antiferromagnetic interaction operated between each pair of nickel ions.

A present study has been reported in regard to bi or tricentered (polymetallic) Schiff base complexes macrocyclic. Schiff base complexes polymeric Schiff base chelates and Schiff base derivatives.

METHODS

The main purpose of the stated that Schiff bases are of immense importance. However, Studies relating to Schiff bases derived from amino coumarins and aromatic aldehydes and their metal complexes are still scanty. With this aim in view physico-chemical studies on the synthesis and characterization of Schiff base complexes of Copper (II) and Nickel (II) derived from substituted coumarins have been undertaken. A metal complexes of the Schiff base with Ni(II) and Cu(II) will be synthesised and characterised the substituted coumarins on MIC.

HYPOTHESIS

Molar inhibitory concentration (MIC), Furan-2-aldehyde 8-amino-7-hydroxy-4-methyl coumarin) and its Metal Ni(II) and Cu (II) complexes

RESULTS

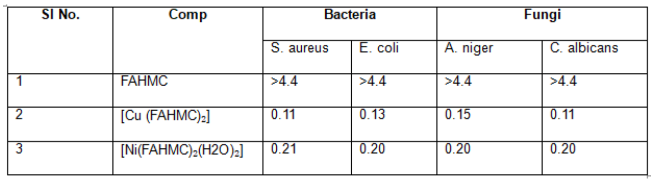
The result will be recorded at various stages and sequence would be drawn. Detailed data will be collected using all possible and suitable methods. Determination of MIC: The sets of two-fold serial dilution of the test compounds are: 1 ml. of the seeded broth (obtained by 1:100 dilution of the indicated microorganisms broth culture in broth) was taken in 100 well-sterilized tubes (3 x 100 mm size) keeping the first tube empty. 2 ml. of each of the seeded broth was prepared having 100 mg/ml and 150 mg/ml of test compounds in tubes A and B respectively (prepared by dissolving 0.2 ml and 0.3 ml of the stock solutions (1 mg/ml) in 1.8 ml and 1.7 ml of broth respectively.

Contents of tube were placed in the first empty tube using a fresh sterilized pipette, 1 ml contents from the B tube were withdrawn and added to second tube and mixed well. Similarly, 1 ml contents from the first tube were withdrawn and added into the third tube and mixed well. 1 ml contents from the third tube were pipetted out with another fresh sterilized pipette and added into the fourth tube and shaken well. This gradient dilution process was continued for all the ten tubes using a fresh pipette each time, 1 ml contents were taken out from the 10 tube and rejected. All the tubes were labelled with 100 mg/ml, 75 mg/ml, 50 mg/ml, 25 mg/ml, 12.5 mg/ml, 6.25 mg/ml, 3.125 mg/ml 1.56 mg/ml, 0.78 mg/ml and 0.39 mg/ml respectively.

1 ml of each of the seeded broth and the broth was placed in two separate tubes for the control of culture and control of broth media respectively in each set of above experiments simultaneously. All the above sets of tubes were incubated in BOD incubator at the desired temperature and time for the respective indicated microorganisms. The tube having the highest dilution showing no visible turbidity was chosen. The amount of the test compound in this tube was the "minimum inhibitory concentration" (bactereostatic concentration). To further ensure the bactericidal concentration, if it is necessary, the subculture from the tube showing no visible growth on agar slants having respective nutrient media and appropriate amount of agar was developed.

Table-1

Molar inhibitory concentration (MIC) in molar concentration (*10*) of FAHMC (Furan-2-aldehyde 8-amino-7-hydroxy-4-methyl coumarin) and its Metal Ni(II) and Cu (II) complexes



Sl No.	Comp	Bacteria		Fungi	
		S. aureus	E. coli	A. niger	C. albicans
1	FAHMC	>4.4	>4.4	>4.4	>4.4
2	[Cu (FAHMC)$_2$]	0.11	0.13	0.15	0.11
3	[Ni(FAHMC)$_2$(H2O)$_2$]	0.21	0.20	0.20	0.20

FAHMC= Furan-2-aldehyde-8-amino-7-hydroxy-4-methyl coumarin

[Cu(FAHMC)$_2$]=Furan-2-aldehyde-8-amino-7-hydroxy-4- methyl coumarin Cu(II)

[Ni (FAHMC)$_2$ (H2O)$_2$] = Aqua furan-2-aldehyde-8-amino-7-hydroxy-4-methyl Ni(II)

Researcher reported the spectroscopic and structural data for [NaCu(CF$_3$COO)$_3$(TEAH3)] (polymeric in the solid state, being a double salt of sodium trifluoroacetate and (triethanolamine)copper(II) trifluoroacetate), [Cu(C$_6$(H$_5$)COO)(TEAH2)]$_2$·2H$_2$O (this compound is simple dimer), [Cu$_3$(CH$_3$COO)$_4$(TEAH2)$_2$]

CONCLUSION

The MIC values of all the synthesized Schiff bases and their metal complexes have been presented in tables-1. The comparative results of biological activity indicate that the complexes of Cu(ll) and Ni(II) are the ligand fragments show much enhanced activity against both the bacterial and also the fungal species as compared with the activity sown by the ligand fragments. FAHMC$_2$[Cu(FAHMC)$_2$] and FAHMC Compound Ni(FAHMC)$_2$(H$_2$O)$_2$] are albicans. A rapid increase in the s. A rapid increas activity of metal complexes than the ligand fragments may be attributed to these factors. More liposolubility of the metal complexes may have increased the activity. The foreign metal ion of the more lipsoluble metal complexes composing the macrocyclic ring may have been replaced by the metal ion present in biological enzymic systems. Thus, rupturing of the enzyme affects a biological system. (trinuclear complexes with Cu$_3$ chains connected by bridging carboxylate and triethanolamine ligands), [Cu$_3$(HCOO)$_4$(TEAH2)$_2$] (trinuclear complexes with Cu$_3$ chains connected by bridging carboxylate and triethanolamine ligands) and [Cu$_3$(CF$_3$COO)$_2$ (TEAH2)$_2$-(CH$_3$OH)$_2$][CF$_3$COO]$_2$ (trinuclear complexes with Cu$_3$ chains connected by bridging carboxylate and triethanolamine ligands) (TEAH3 = triethanolamine (N(CH$_2$CH$_2$OH)$_3$); [TEAH2] = mono-deprotonated ion; [TEAH]$_2$ = doubly deprotonated ion). Researchers employed direct reaction of copper(II) carboxylates with TEAH3 and reaction of the tetrameric compound [{Cu(TEAH)}$_4$] with copper(II) carboxylates. The magnetic behavior of the dinuclear and trinuclear species was investigated and suggests that at low temperatures the metal centers exhibit strong ferromagnetic coupling, that switches to simple paramagnetic behavior on warming. The complex Na$_2$[Cu$_2$(H$_5$)(OH)].11H$_2$O as shown in Figure 27 (H$_5$ is the Schiff base prepared by condensation of 2,6-diformyl-4-chlorophenol and 1-aminoethane phosphonic acid in the presence of NaOH) is an example of [1+2] end-off acyclic complexes as suggested by Vitago et.al. 2004. In this complex the copper ions was five coordinated square pyramidal where a phenolate oxygen gave the endogenous bridge while an OH$^-$ group gave the exogenous one and two water molecule was in the apical positions.

The combined activity of the ligand molecule and the metal ion may have multiplied the biocidal effect. The more rapid penetration of the metal complexes as a whole through the cell walls of the microorganisms causing damage to the protein synthesis and nucleic acids.

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