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Synthesis, Structural Characterization, and Antibacterial Activity of Iron (II) New Schiff-Bbase Compounds

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Abstract

A binuclear Schiff base ligand undergo condensation with Glycyl glycine and O-pthalaldehyde, and the condensation product reacts with binuclear metal complexes [M2(L)(H_2O)4] where M=Fe(II), the Schiff base serves as an octadentate N4O4 ligand, which is used to coordinate with the binuclear Fe(II) metal centers. The Ligand and the metal complexes are characterized by the elemental analysis, conductivity measurements, magnetic susceptibilities, Infrared, ^{1}H and ^{13}C NMR, Mass spectra, Electronic spectroscopies and TGA analysis. ESR Spectra provided further information to confirm the binuclear structures. The metal complexes show good antibacterial activity against Gram-positive and Gram-negative bacteria.

Keywords: ***Binuclear complexes; Schiff base synthesis; Structural characterization; Antibacterial activity.***

Introduction

The condensation of primary amine with either an aldehyde or ketene yields Schiff base [2-4] and these Schiff bases have many applications and uses, in many areas such as have a biological, clinical, and pharmaceuticals etc. The synthesis and application of Schiff bases and their coordination compounds have been highly considered in many chemical and biological fields [5-10] amino acids containing imines are biologically significant [12,13], they easily form more stable complexes with most transition metal ions [14]. Recently many scientists focused on the chemistry of amino acids of Schiff bases containing oxygen, nitrogen and donor atoms containing metal complexes for the physiological reasons [15,16]. The design and synthesis of symmetrical Schiff-bases, derived from the 1:2 stepwise condensations of carbonyl compounds. With many organic alkyl or aryl amines. And a wide range of aldehyde or ketone functionalities, as well as their Fe (II) complexes have been of interest due to their preparative accessibility, structural variability and tuneable electronic properties allowing to carry out systematic reactivity studies based on ancillary ligand modifications, And to mimic bimetallic biosites in various proteins and enzymes [17-25]. Fe(II) complexes thus play an important role in developing the coordination chemistry, catalysis, and

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enzymatic reactions, magnetism and bioinorganic modelling studies [26,27] etc. In this regard, there is much current interest in designing binucleating ligands and their transition metal complexes [23,28].

Shakir and Verkey [29], Al-Kubaisi [30], Geeta [31,32] have also reported on the synthesis characterization of macrocyclic binuclear metal complexes by template condensation of many acids, Similarly, the binuclear complexes have been prepared and characterized and developed various co-ordination compounds including Schiff-base macro cycles derive from o-Phthalaldehyde and different amines. And also they did excellent catalytic and antibacterial activity of the macro cyclic Schiff-bases and their metal complexes [31,32]. With Schiff-base produced from condensation reaction of o-Phthalaldehyde with glycyl-glycine (SCHEME 1). A description on characterization data using analytical, spectroscopic, thermal and magnetic data has been systematically presented. Furthermore, the application of these metal complexes as potential antibacterial agents has also well explained.

Experimental Methods

Instruments

Melting points of all the ligands and complexes were determined on a Buchi-510 melting point apparatus. The percentages of carbon, hydrogen, nitrogen in macro cyclic Schiff base metal compounds were determined by using a Perkin-Elmer 240C CHN analyzer. UV-Visible spectra were recorded with Shimadzu UV-160A, a UV-Visible double beam spectrophotometer with matched quartz cell of 1-cm path length, The IR spectra in KBr pellets were recorded on Perkin Elmer-283 spectrophotometer the scanning time was 6 min in the range of 4000-200 cm^{-1}. Brucer WH 300(200 MHz) and Varian Gemini (200 MHz) spectrometers were used to record 1H NMR and 13C NMR spectra. MICROMASS-7070 spectrometer operating at 70 ev using a Gouy balance calibrated with Hg $[Co(NCS)_4$ was used to determine magnetic susceptibilities of complexes in EtOH at room temperature using Digisun Digital conductivity meter model-909. The antibacterial activity of the compounds was determined by the cup plate method and minimum inhibitory concentration by liquid dilution method [33,34].

Materials

Iron salts, Ortho-pthalaldehyde, amino acids and other chemicals were purchased from Aldrich, USA and all the compounds are analytical grade. The solvents were distilled and stored over molecular sieves. The purity of compounds was checked by TLC using Merck 60F254 silica gel plates. The antibacterial activity of the compounds was determined by the cup plate method and the minimum inhibitory concentration by liquid dilution method [33,34]. The eight amino acid Schiff base lignds, *viz.*2-{[(E)-1-1-(2-{[C1-carboxyethyl)imino]methyl]phenyl}phenyl) methylidene] amino} propanoic acid (CEIMPA),

2-{[(E)-1-(2-{[C1-carboxy -2-Carboxyphenylethylimino] methyl} phenyl)methylidene] amino}-3-phenyl propanoic acid(CPEIAP).,2-({(E)-1-[2-({1-carboxy 2-4 hydroxyphenyl)ethyl]imino}methyl)phenyl]methylidene} amino)-3-(4-hydroxyphenyl) propanoic acid(CPEIMP).

2-({2-[(E)-1{2-[(carboxymethyl)amino]-2-oxoethyl}imino]methyl}phyenly)methylidene)amino)acety)amino)actic acid (CMAIPA).

2-({(E)-1[2-({[1-carboxy-2-(3,4-dihydroxyphenyl)-1- methyl/ethyl]imono}methyl)phenyl]methylidene}amino)3-(3,4-dihydroxyphenyl)-2-methyl propanoic acid (CPMIMP)., 2-{[(E)-1-(2-{[1,3dicarboxypropyl)imino]methyl}phenyl]methylidene}amino)pentanedioic acid (DCPIMP), 2-({(E)-1-[2-({[1-corboxypropyl-2-(1H-3-indoly)ethyl]imino}methyl)phenyl]methylidene}amino)--(1H-3-indolyl)propanoic acid (CEIMAP), 2-({2-[(E)-1{2-[(carboxy-2-(1H-5- imidazolyl)ethyl)imino]methyl}phenyl]methylidene}amino)-3-(1H-5imidazolyl)propanoic acid(CIMPAP).were prepared as previously [43,44].Our synthetic route of Schiff-base ligand is shown in SCHEME 1.

2-(2-[((E)-1-2-[(2-{(carboxymethyl) amino] oxoethylimino) methyl]phyenly)methylidene)amino]acetylamino) acetic acid(L) (CMAIPA)

Yield 74%; mp 196-198; IR 3318,2918,2842,1720,1643,1632,1570,1128cm -1:1H NMR(200 MHz, DMSO) in ppm.11.56(s,2H,COOH),8.19(s,2H,CH=N),7.22-7.54(m,4H,Ar-H),5.83(s,4H,CH_2),5.60(s,2H,NH),4.25(d,4H,CH_2):13CNMR(67.93MHz,DMSO) 48.5(2C,CH_2),58.3(2C,CH2),130.6,132.3,136.4(6C,ArC),163.7(2C,CH=N),171.2(2C,C=O),180.4(2C,COOH)al. Found:C,53.04;H,5.01;N,15.48%.Calcd. for C16H18N4O6:C,58.84:H,4.94:N,15.46%MS:[M]+ at m/z362 in TABLE 1.

TABLE 1. **Physical analytical data of the ligand and complexes.**

Complex/molecular formulae	**Color**	**Yield (g)**	**Found (Calculated) (%)**			
			C	**H**	**N**	**M**
$[Fe_2L(H_2O)_4]_3H_2O$ $C_{16}H_{32}N_4O_{13}Fe_2$	Pale green	0.418(70.2)	35.31(35.38)	5.93(5.98)	10.29(10.36)	10.26(10.34)

Synthesis of metal complexes

A solution of Iron (II) acetate (0.002-0.005 mol) in methanol (25 mL) was added drop wise to a methanolic solution (30 mL) of Schiff base (0.002-0.005 mol) with constant stirring at room temperature. The resulting mixture was allowed to reflux on a water bath for 2 h until a solid is separated out. The precipitates were suction filtered, purified by repeated washings with chloroform and methanol and dried in vacuum desiccators (70-80%).

Result and Discussion

All the complexes are soluble in methanol and water. The elemental analysis data and the physical properties of the complexes are listed in TABLE 1.The complexes can be represented as The formula [M2L(H_2O)4].3H_2O whereas (M=Fe(II),

(L=ligand). The molar conductances values of the complexes are measured in dichloromethane at 10-3 M concentration are in the range of 8-19 indicate that all the complexes behave as non-electrolytes [16].

I.R spectra

All the infrared spectral frequencies of the Schiff base ligands and its Fe (II) are given in the TABLE 2. All the complexes exhibit broad bands in the range of 3442-3566 cm^{-1}, and this may be accredit to the presence of coordinated or lattice water molecule. A strong IR absorption band appears in the free Schiff base around 1563-1600 cm^{-1} assignable to the vasym (COO) absorption of ligands was shifted to higher range of frequency in the 1576-1589 cm^{-1} range and the vsym (COO^{-1}) visualizes the combining of carboxyl oxygen to the metal ions along with imino nitrogen atom [35]. In the low frequency regions. Bands detected around 516-538 cm^{-1} ranges are assigned to M-N (imino nitrogen) and the bands at 420-480 cm^{-1} ranges are assigned toM-O (carboxyl ate oxygen atom) [36-39]

NMR spectra

Further evidence for the presence of combination of Schiff base ligands in the Metal complexes is provided by the proton NMR spectra of the complexes (TABLE 2). The integral intensities of each and every signal were found to concur with the number of different types of protons present in the complexes. A signal appeared in the ligand ^{1}H – NMR spectrum at 8.18 is due to CH=N protons. However, in the spectra of Fe (II) complex the signal moved down field at 8.22 suggests the coordination of imino nitrogen to manganese ion [40] carbonyl proton of the ligand was observed at 11.53 ppm. However it was not present in the complex spectrum due to the involvement of carboxyl oxygen in chelation through deprotonation [41]. Further, a broad signal found in the complex spectrum at 6.2 ppm corresponds to NH proton, which was shifted from 5.66 ppm of ligand give evidence to the coordination of NH group [25].

^{13}C NMR Spectral analysis

In the ^{13}C spectra of Fe (II) complexes a down field shift of CH=N group was observed in between 168.9- 176.8.ppm and for carbonyl carbon at 193.9 ppm it signifies that the ligand coordinates through the nitrogen atom of CH=N[42] and through the oxygen of carboxyl group of the ligand [42,43]. Furthermore, the down- field of shifting of amide adjacent carbonyl (C-O) describes the coordination of this site to manganese ion, however, the enolic carbon peak shifted to 108.6-116.4 suggesting that coordination of C-O group to the metal by DE protonation. The proton NMR and ^{13}C NMR spectrum of [Mn2L]. Binuclear complex is given in SCHEME 1.

Electronic spectra

In binuclear Fe (II) complexes the electronic spectral broad bands are in the range14,326 and at 13,853 cm^{-1}. The erstwhile band may be due to the spin forbidden transition 6A1g-4T2g (G), which may gain intensity as a result of the vibronic mechanism in the octahedral field around ferric ion. The second bands may be assigned to 6A1--4T1 (G) transitions [44]. Moreover a third absorption band with high intensity observed at 25,252 cm^{-1}. Allocate to a charge transfer transition. The

magnetic moment of the complex is 7.42-7.47 B.M. This value is low compared to the calculated magnetic moment value for binuclear ion complex [44] (FIG. 1).

SCHEME 1: **Synthetic route of binuclear metal (II) complexes.**

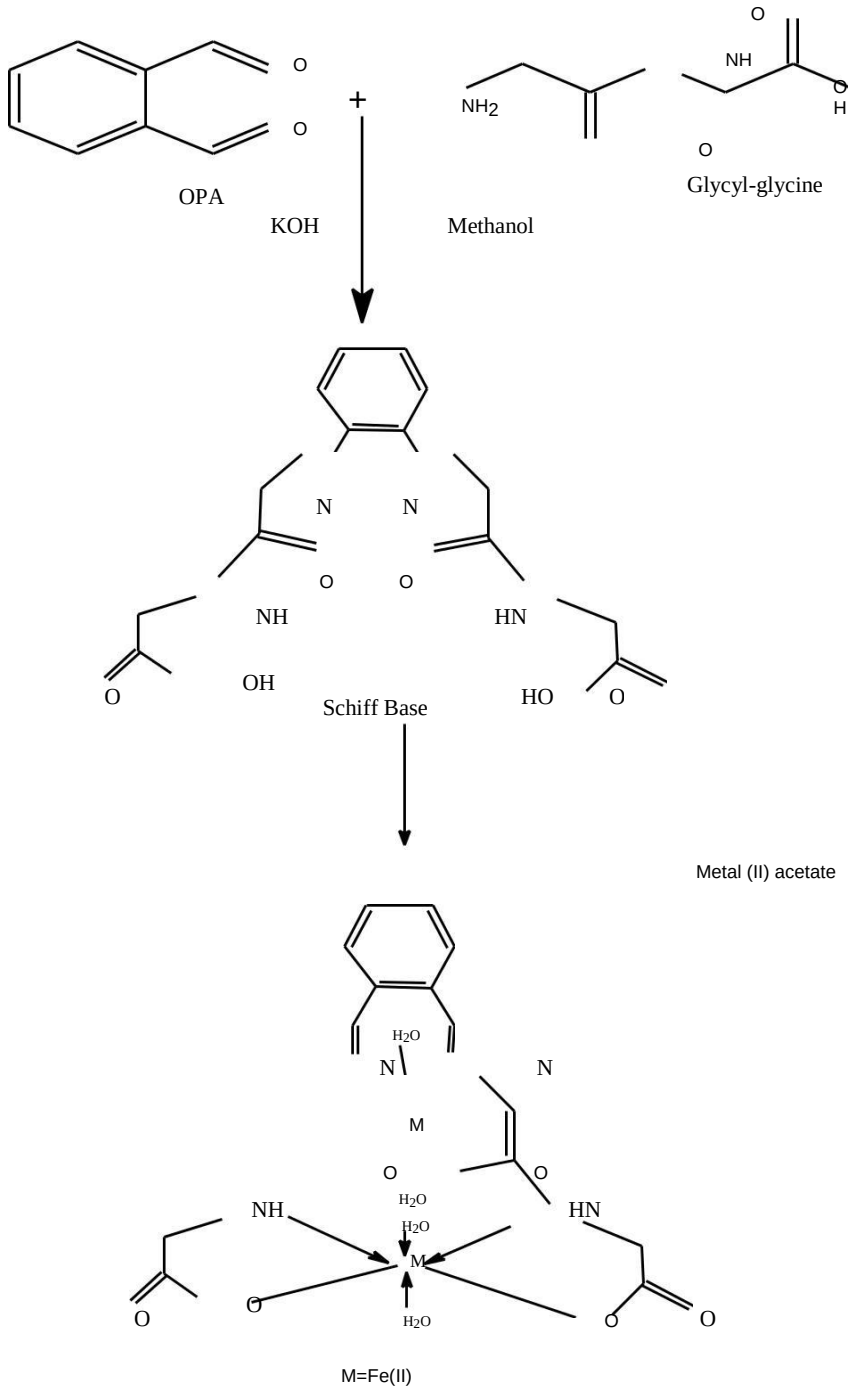


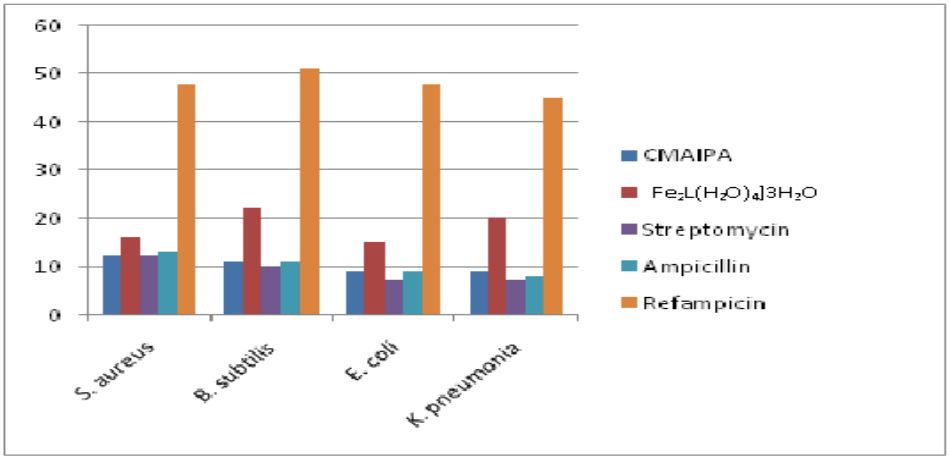
TABLE 2. **Electronic spectral band and magnetic moments (B.M.)**

Complexes		
$[Fe_2L(H_2O)_4]^3H_2O$	14326,13853,25,252	7.42-7.47

TABLE 3. **Zone of inhibition of CMAIPA and its Fe (II) complexes against different bacteria**.

Ligand/Complexes	**Zone of inhibition (mm)**			
	Gram positive bacteria		**Gram-negative bacteria**	
(1000 µg/mL)	***S. aureus***	***B. subtilis***	***E. coli***	***K. pneumonia***
CMAIPA	12	11	9	9
$Fe_2L(H_2O)_4]^3H_2O$	15	21	14	19
Streptomycin	12	10	7	7
Ampicillin	13	11	9	8
efampicin	48	51	48	45

FIG.1. **Comparison of MIC Values (1000 mg/ml) of complexes and standard drugs against different bacteria.**



Anti-bacterial activity

Anti-bacterial activity of the ligand CMAIPA and its Fe(II)complexes against two Gram- positive (*B. Subtilis* and *S. aureus*) and two Gram-negative (*E.Coli* and *K. pneumonia*) bacteria were studied using three existing antibacterial drugs *Viz.* streptomycin, ampicillin and rifampicin. Preliminary screening for the complexes was performed at the fixed concentration of 1000 µg/mL. Inhibition was recorded by measuring the diameter of the inhibition zone at the end of 24 h for bacteria. Among the compounds tested with the Fe(II) metal complexes showed good inhibition towards all tested strains TABLE 3. The activity of all these complexes µ were further confirmed by determining the minimum inhibitory concentration 33,34,44.values by liquid dilution method in which the effectiveness was observed at lower concentrations. The comparison of MICS of all the complexes and standard drugs against tested strains are presented in FIG. 1. it was found that Fe(II) Complexes have good activity against all bacterial strains with MIC value, in particular Fe(II) complex showed excellent activity R against all the bacterial strains even than standard drugs streptomycin and ampicillin the results from these studies have also shown that complexation of metal to CMAIPA serves to improve the antimicrobial of the ligand. This higher antibacterial activity of the metal complexes compared to ligand is may be due to the changed in structure due to coordination and chelating trend to make metal complexes acts as more powerful and potent bacteriostatic agent, thus inhibiting the growth of the bacteria. Furthermore, chelation reduces the polarity of the metal ion mainly due to the partial sharing of its positive charge with the donor group within the chelate ring system. Such chelation increases the lipophilic nature of central metal atom, which favour its permeation more efficiently through the lipid layer of the microorganism, thus destroying them more forcefully. Thus all the complexes showed more increased activity than the corresponding ligand and two antibacterial drugs. The activity of ligand, complexes standard drugs against different bacteria were found to be CMAIPA (L) < S treptomycin < Ampicillin is less than $Fe^{2}L\ (H_2O)^{4}3H_2O$< Rifampicin for *B.subtilis*, streptomycin<CMAIPA(L)= Ampicillin< rifampicin for *E.coli* and streptomycin < Ampicillin<CMAIPA(L)<rifampicin for *K. Pneumonia*.

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