Available on line www.jocpr.com

Journal of Chemical and Pharmaceutical Research

ISSN No: 0975-7384
CODEN(USA): JCPRC5

J. Chem. Pharm. Res., 2011, 3(1):382-387

Antimicrobial activity of some of chlorocobaloximes containing axial substituted pyridines

M. Amutha selvi[a] , P.Jothi[a], A. Dayalan[a]*,V. Duraipandiyan[b] and S. Ignacimuthu[b]

[a]*Department of Chemistry, Loyola College (Autonomous), Chennai, INDIA*
[b]*Entomology Research Institute, Loyola College(Autonomous), Channai, INDIA*

ABSTRACT

Cobaloximes of the type [Co(dmgH)$_2$(B)Cl] ; where, dmgH$^-$ = dimethyl glyoximate, B= 3-chlorpyridine (3-PyCl), 3-bromopyridine (3-PyBr), 4-aminopyridine (4-AP), 4-methylpyridine (4-MP), 4-N,N'-dimethyl aminopyridine (4-DMAP) and 4-cyanopyridine (4-PyCN) were prepared, characterized by the usual spectroscopic techniques and screened against microorganism for antimicrobial activity with ciprofloxacin as standard. The cobaloximes were found to be active against most of the microbes. The cobaloxime containing 4-cyanopyridine as the axial ligand showed potential inhibition; whereas, the complex [Co(dmgH)$_2$(3-PyCl)Cl] showed the least microbial growth.

Key words: Cobalt(III) complexes, cobaloximes, antimicrobial activity of cobalt(III) complexes.

INTRODUCTION

The cobaloximes are of interest from both chemical and biological [1] point of view as they are closely related to vitamin-B_{12} [2-4]. Coenzymes-B_{12} have been studied and reviewed in the last three decades [5] due to their function as biological catalysts [6] and as templates in organic synthesis [7-15]. Pyridine derivatives play significant role in many biological systems as the component of several vitamins, nucleic acids, enzymes and proteins [16]. But, their studies on the antimicrobial activities as their metal complexes are rare in literature. Metal complexes containing nitrogen and sulphur donors have been proved to be potential antibacterial and fungial agents [17] as well as component of several vitamins and drugs [18, 19]. The present study deals

with the preparation and characterization of cobaloximes of the type *Trans*-[Co(dmgH)$_2$(B)Cl] and their antimicrobial activity.

EXPERIMETAL SECTION

Materials and methods

Cobalt(II) chloride, dimethyl glyoxime and the various substituted pyridines (purchased from SD Research Laboratory) were used for the preparations of the complexes. Dimethyl sulpoxide was dried over calcium hydride and distilled at reduced pressure. The distilled solvent, stored under molecular sieves, was used for the study of the antimicrobial activity.

Preparation of the cobaloximes

The green dicholoro cobalt complex: H[Co(dmgH)$_2$Cl$_2$], was prepared as reported in the literature [20,21]. About 0.005 moles of the above complex, in ethanol, was stirred for 10 minutes with 0.005 moles of the ligands [viz., 3-choloro pyridine, 3-bromo pyridine, 4-amino pyridine, 4-methyl pyridine, 4-N,N'-dimethylamino pyridine, 4-cyanopyridine] in different lots. The reaction mixtures were refluxed for about 2-3 hrs at 40^{o}C and allowed to settle for 1 hr, after which the brown colored products were collected in a glass sintered crucible, washed successively with ethanol, ether and finally dried in vacuum desicator.

Spectral Studies

The UV–Visible spectra of the complexes were recorded on LAMDA-25 spectrophotometer using 1 cm matched quartz cells in aqueous ethanol of suitable concentrations. The IR spectra were obtained using PERKIN ELMER FTIR spectrophotometer using KBr pellets and the ^{1}H NMR spectra were recorded on JOEL 400 MHz NMR spectrometer using DMSO-d$_6$ as solvent.

Antimicrobial activity

In vitro antimicrobial activities of the complexes were determined using different microorganisms by disc diffusion method . The microbial strains such as *Staphylococcus aureus* (MRSA), *Salmonella paratyphi*-B, *Malassezia pachydermatiis*, *Shigella flexneri* MTCC-1457, *Candida krusei*, *Staphylococcus aureus* MTCC-96, *Staphylococcus epidermidis* MTCC-3615, *Candida parasilopsis* etc., were obtained from the Institute of Microbial Technology, Chandigarh, India and the yeast cultures were obtained from the Department of Microbiology, Christian Medical College, Vellore, INDIA

Preparation of inoculums

The bacterial inoculums were prepared by growing the cells in Mueller Hinton Broth, MHB, (Himedia) for 24 hrs at 37°C. These cell suspensions were diluted with sterile MHB to provide initial cell counts of about 10^4 CFU/ml. Yeast was grown on Sabouraud Dextrose Broth (SDB) at 28^{o}C for 48 hrs.

Disc diffusion method

Petri plates were prepared with 20 ml of sterile Mueller Hinton Agar (MHA) (Hi-media, Mumbai). The test cultures were swabbed on top of the solidified media and allowed to dry for 10 min. The complexes were dissolved in DMSO and 25 µl of the complexes were loaded per disc. The loaded discs were placed on the surface of the medium and left for 30 min at room

temperature for diffusion. Negative control was prepared using respective solvent [22]. Ciprofloxacin (10µg /disc) was used as positive control. The plates were incubated for 24 hrs at 37^{o}C for bacteria and 48 hrs at 30^{o}C for yeast. The zone of inhibitions were recorded in millimeters. All such experiments were repeated thrice.

RESULTS AND DISCUSSION

The dichlorocobaloxime, H[Co(dmgH)$_2$Cl$_2$], is an intense green crystalline compound [16] which turns brown on treatment with heterocyclic donors like pyridine [23]. A similar color change with the substituted pyridines used shows that their activity towards dichlorocobaloxime is similar to that of pyridine.

UV-VISIBLE Spectra

The UV spectra of the cobaloximes showed a shoulder around 330 nm which may be due to the ligand to metal charge transfer (LMCT) [24]. The electronic spectra of the complexes showed an high intense absorption band in the range 230-270 nm which may be attributed to $\pi \rightarrow \pi^*$ transition of the pyridine ring [25]. The moderately intense band around 245-260 nm, may be ascribed to $\pi \rightarrow \pi^*$ transition of dmgH$_2$ [26].

IR Spectra

Rubin *et al* [27], have reported the stretching and bending frequencies for similar complexes. The peak around 1090 cm^{-1} was assigned to N-O stretching [28]. This band was shifted to lesser frequency when the axial ligands were bonded to central cobalt ion. The band around 515 cm^{-1} can be assigned to Co-N stretching between cobalt(III) and nitrogen atoms of dimethylgloxime. All the complexes show a weak broad band around 3450 cm^{-1} corresponding to hydrogen bonded O-H of dmgH$_2$ [29].

The band in the range 980-1020 cm^{-1} may be attributed to deformation vibration of OH of dmgH$_2$ and the band at 685-750 cm^{-1} is due to C=N-O deformation vibration. The bands at 1395 and 1240 cm^{-1} are due to asymmetric and symmetric deformation vibrations corresponding to the methyl group of dimethylgloxime respectively. The peak at 1560 cm^{-1} due to the C=N stretch of dmgH$_2$ [30] shifts to lesser frequency.

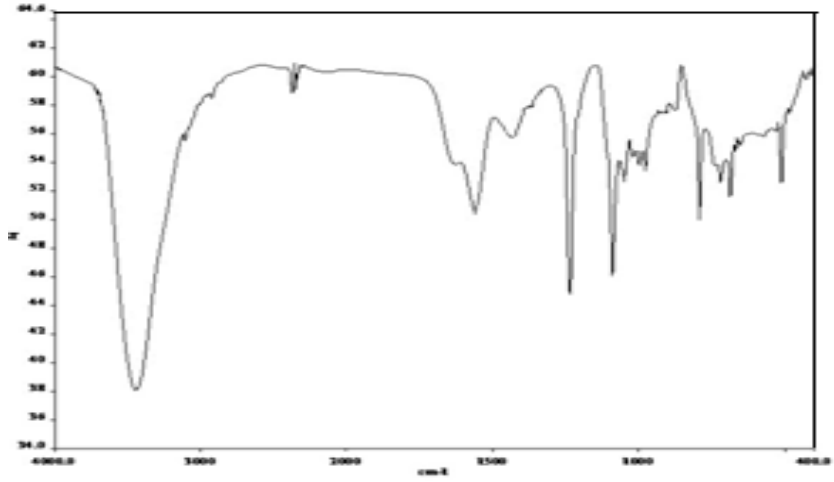

Fig-1: IR Spectrum of [Co(dmgH))$_2$(3-PyBr)Cl]

^{1}H NMR Spectra

The methyl protons of dimethylglyoxime, in all the cobaloximes, appears as a sharp singlet at 2.4 ppm(12H) [29]. A peak at 8.3 ppm indicated the O-H proton of the oxime (2H). A peak appearing at 2.46 ppm may be assigned to 6 methyl protons of the 4-N, N'- dimethyl aminopyridine . The signals in the range of 7-8 ppm, may be due to the pyridine ring of the substituted pyridine at the axial position of the complexes [23].

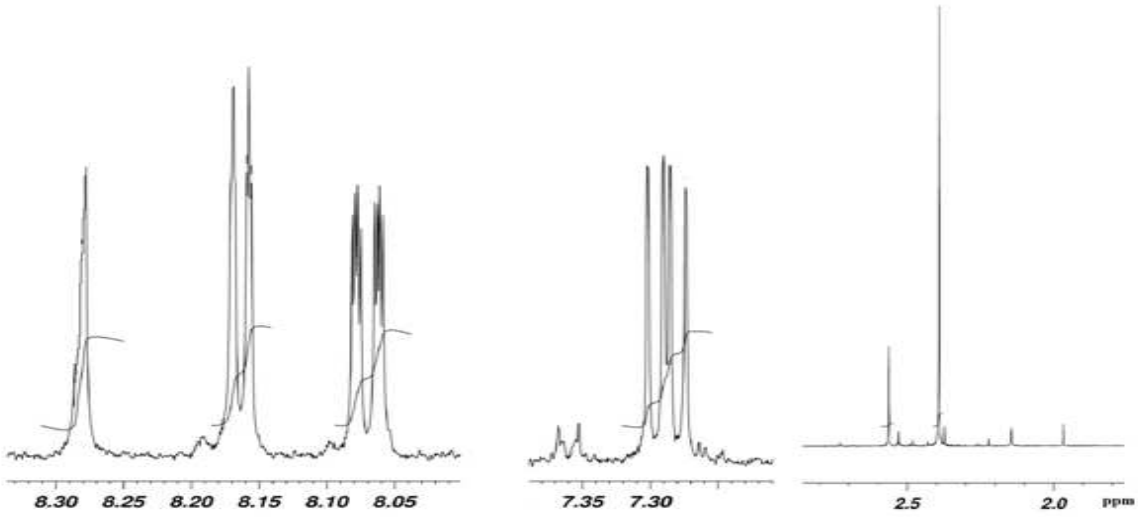

Fig- 2: ^{1}HNMR Spectrum of [Co(dmgH)$_2$(3-PyBr)Cl]

Fig-3: Antimicrobial activity of cobolaximes
{*S. epidermidis*(3615) and *S.flexneri* (109)}

Antimicrobial activity

All the complexes exhibited varying antimicrobial activity towards most of the microbes selected (Table-1) and were found to be dose dependent. Most of the complexes inhibited moderate growth of *S. epidermidis, C. parasilopsis* and *S. aureus* (MRSA). The complex-1 inhibited the growth of *S. epidermidis* (8 mm), *S. flexneri* (8 mm) and *C. parasilopsis* (8 mm) (Fig-3). The same complex did not inhibit the growth of other micoorganisms. The complexes 2, 4, 5 and 6 showed moderate activity towards all the microbes except very few. All the complexes

significantly inhibited the growth of *S. epidermidis* and *S. flexneri*. The maximum inhibition zone was observed in complex-6 against *Malassezia pachydermatiis* (17 mm), *Staphylococcus epidermidis* (16) and *S. flexneri* (16 mm).

Table:1-Antimicrobial activity of the cobalaximes against pathogenic microbes at 200 µg/disc

Organisms	Zone of inhibition in (mm) For *Complexes 1 to 6						Control
	1	**2**	**3**	**4**	**5**	**6**	Ciprofloxacin 10µg/disc
Staphylococcus aureus (MRSA)	-	12	10	12	17	15	15
Salmonella paratyphi-B	-	8	-	-	-	10	32
Malassezia pachydermatiis	-	-	-	12	12	17	21
Candida krusei	-	12	-	12	-	-	-
Staphylococcus aureus	8.5	8.5	8	10	12	12	30
Staphylococcus epidermidis	8	10	10	10	12	16	30
Candida parasilopsis	8	8	8	-	8	8	-
Shigella flexneri	8	10	8	10	12	16	12

- : No activity
Ciprofloxacin – Antibacterial agent

**** Complexes:***

1. *[Co(dmgH)$_2$(3-PyCl)Cl] ;* ***2.*** *[Co(dmgH)$_2$(3-PyBr)Cl] ;* ***3.*** *[Co(dmgH)$_2$(4-AP)Cl] ;*
4. *[Co(dmgH)$_2$(4-MP)Cl] ;* ***5.*** *[Co(dmgH)$_2$(4-DMAP)Cl] ;* ***6.*** *[Co(dmgH)$_2$(4-PyCN)Cl]*

Most of the complexes did not inhibit the growth of *S. paratyphi*- B and *C. krusei*, except for [Co(dmgH)$_2$(3-PyBr)Cl], [Co(dmgH)$_2$(4-MP)Cl] and [Co(dmgH)$_2$(4-PyCN)Cl]. The antimicrobial activity order observed was [Co(dmgH)$_2$(4-PyCN)Cl] > [Co(dmgH)$_2$(3-PyBr)Cl] > [Co(dmgH)$_2$(DMAP)Cl] > [Co(dmgH)$_2$(4-MP)Cl]. Among the complexes, cobaloxime containing 4-cynaopyridine as the axial ligand showed potential inhibition of bacterial growth.

The activity of the complexes can be explained on the basis of chelation theory. On chelation , the polarity of the metal ion may 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 electrons over the whole chelate ring and enhances the penetration of the complexes into lipid membranes blocking the metal binding sites in the enzymes of microorganisms. These complexes may also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism [31]. Hence, it may be concluded that cobaloximes will show antimicrobial activity depending on the nature of the axial ligands.

Acknowledgement
The authors are thankful to Rev.Fr. B. Jeyaraj, *Principal*, Loyola College, for providing the necessary facilities. The Head, SAIF, IIT, Madras for recording NMR Spectra.

REFFERENCES

[1] E. Jona ; M. Kubranova; R Simon and J Mrozinski. *J. Thermal Anal*., **1996,**46, 1325.
[2] P Michel; M Jenson Diana Zinki and J Halpern. *Inorg.Chem*., **1999,** 38, 2386.

[3] T Brown; A Dronsfield and AS Wilkinson. *Inorg.Chem.Acta*., **1997,** 262, 97.
[4] DG Brown. *Progr.Inorg.Chem*., **1973,** 18, 177.
[5] N Bresciani-Pahor; M Forcoline; LG Marzilli; L Randaccio; MF Summers and PJ Tosacano. *Coord. Chem. Rev*., **1985**, 63, 1.
[6] S Nemeth and L Simandi. *J. Mol. Catal*., **1982**, 12, 87.
[7] Giese B. Radicals in organic synthesis formation of carbon-carbon bond, Oxford Pergamon, **1986**; 320.
[8] R Scheffold; G Rytez and L Walder. *Trans.Met. Org. Syn.*, vol. 3, Chichester: Wiley, **1983**.
[9] AK Ghosh and Y Chen. *Tetrahedron Lett.*, **1995**, 505.
[10] M Wright and ME Welke. *J. Org. Chem*., **1996**, 61, 133.
[11] BD Gupta; V Singh; K Qanungo; V Vijakanth and R S Sengar. *J. Organomet. Chem.*,**1999**, 582**,** 279.
[12] BD Gupta; V Dixit and J Das. *J. Org. Met. Chem*., **1999**, 572, 49**.**
[13] T Brown; A Dronsfied; A Jablonski and AS Wilkinson. *Tetrahedron Lett*.,**1996**, 37, 5413.
[14] GB Gill; G Pattenden and GA Raon. *Tetrahedron Lett*.,**1996**, 37, 9369.
[15] L Gage and BP Branchaud, *Tetrahedron Lett*., **1997**, 40, 7007.
[16] SC Nayak ; PK Doss ; and K Sahoo. *J.Anal.Appl.Pyrolysis*., **2003**, 70, 699.
[17] J Crim and H Petering, *Cancer Res.*, **1967**, 27, 1278.
[18] M Kato and Y Muto. *Coord. Chem. Rev*., **1988**, 92, 45.
[19] R Nagar. *J. Inorg. Biochem*., **1990**, 40, 349.
[20] G Costa; G Mestroni and L Stefani. *J.Organo.Met.Chem*, **1967**, *7*, 493.
[21] P Jothi; C Revathi; A Dayalan; P Ramesh and A Subiapandia. *Acta Cryst*., **2008,** *E64*, m300.
[22] WL Drew; AL Barry; R O'Toole and JC Sherris. *Appl. Environ. Mirobial*., **1972**, 24, 240.
[23] NB Phor; M Forocolin; PJ Toscano; MF Summers; L Randaccio and LG Marzilli. *Coord. Chem. Rev*., **1985**, 63, 1.
[24] S Martin and A Dayalan., *Indian J. Sci. Technol.*, **2009**, 2(9), 59.
[25] A Dayalan and C Revathi., *J. Serb. Chem. Soc.*, **2006**, 71(12), 1311.
[26] Bakheit Mustafa Mohamed Salih and S Satyanarayana., *Afr. J. Pure Appl. Chem.*Vol., **2009**, 3(9), 170.
[27] J.M Rubin-Preminger; U Englert. *Inorg. Chem. Acta*, **2009**, *362*, 1135.
[28] R Bline and D Hadzi, *J. Chem.Soc.*, **1958**, 36,45.
[29] RM Silverstein, GC Bassler, TG Morrill. Spectrometric Identification of Organic Compound, 5th Edition, Wiley, **1991**; 111.
[30] NS Biradar and VH Kulkarni. *J. Inorg. Nucl. Chem*., **1971**, 33, 2451.
[31] N Harmaraj; P Viswanathamurthi; K Natarajan. *Trans. Met .Chem.*, **2001**, 26,105.