Journal of Medical Sciences

ISSN 1682-4474

science alert

ANSInet
an open access publisher
http://ansinet.com

Research Paper

J. Med. Sci., 3 (4): 289-293
July-August, 2003

Antimicrobial Studies of Mixed Ligand Transition Metal Complexes of Maleic acid and Heterocyclic Amine Bases

M. Saidul Islam, Md. Belayet Hossain and Md.Yeamin Reza

Mixed-ligand transition metal complexes of Co (II) ions were synthesized, where, Maleicacid as a primary ligands and heterocyclic amine bases as a secondary ligands have been used, respectively. Moreover, mixed-ligands transition metal complexes of Fe (III) ions were also synthesized by the same way. Their conventional physical and chemical analysis has been done. Their anti-bacterial and anti-fungal activity has been evaluated. Disc diffusion methods were employed for anti-microbial assays against 14 pathogenic bacteria (5 g positive and 9 g negative) and 14 fungi. The complexes containing 8-hyroxy-quinoline as secondary ligand were much more microbial activity than the other complexes. In addition, the complexes K[Co(II)(ME)(8-HQ)] shows the highest anti bacterial activity against all bacterial tasted (when, ME=C_4 H_2O_4 and 8-HQ=C_9H_6NO).

Key words: Biological activity, maleicacid, heterocyclic amine bases mixed ligands complexes

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publish original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued six times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

M. Saidul Islam
Professor
Department of Chemistry
University of Rajshahi
Rajshahi-6205
Bangladesh

ANSInet
Asian Network for Scientific Information

Department of Chemistry, Rajshahi University, Rajshahi-6205, Bangladesh

Introduction

Synthetic chemical compounds constitute important sources of various bioactive compounds as antibacterial (Zakaria ***et al.***, 2000) antifungal (Islam ***et al.***, 2000) and anticancer (Pratt, 1979, e.g. Cisplalin) compounds. The synthesized chemical compounds which, are used for the treatment of infectious diseases are known as chemotherapeutic agents. Every year thousand of compounds are synthesized with an aim to find a potential chemotherapeutic agent combat pathogenic microorganisms. Fe(III), Ni(II), Co(II) and Cu(II) complexes with thiazoline and their fungicidal activity has been evaluated (Sangal ***et al.***, 1994). Eight salicylhydroxamic acids and their 56 metal chelates with Cu(II), Ni(II), Co(II), Fe(III), Mn(II) and Zn(II) were screened for their antifungal activities which exhibited that chelates are more active than the parent salicylhydroxamic acids being maximum for metal chelats of Co(II) with halo and nitro substituted salicylhydroxamic acids (Khadikar ***et al.***, 1994). On the weather resistance of specimens treated with a mixture of tall oil and maleic anhydride in a one year exposure test and a 670 h ageing process. The treatment inhibited the growth of blue stain and mould fungi (Paajnar ***et al.***, 1999). Heterocyclic bases have a great important in biological and industrial fields most of the heterocyclic bases are used as corrosion inhibition an as anti-bacterial, anti-convulsive, anti-fungal and anti-fouling agent. The chlorinated species of 8-hydroxyquinoline has been proved as antibacterial and antifungal agent (Mayer ***et al.***, 1980) and the di-iodo derivative is administered to overcome Zn deficiency in animal (Dell, 1980). Derivatives of Cu with 8-hydroxyquinoline are anti-fouling agents (Nakazawa ***et al.***, 1980) and it itself protects the industrial and fungi in them (Kulieve ***et al.***, 1979b) 3-Aminophyridine has strong anti-convulsive effects (Baranyi ***et al.***, 1979; Szente ***et al.***, 1984).

Some mixed ligand complexes of Co(II) and Fe(III) ion with maleicacid (MEH_2) as primary and heterocyclic bases viz: quinoline(Q), iso-quionoline(IQ), 8-hydroxyquinoline(8-HQ), Pyridine(py), 2-aminopyridine(2apy) and 4-picoline (4-Pico) as secondary ligands have been prepared and their anti-microbial studies have been carried out.

Materials and Methods

Preparation of the Co(II) complexes

The freshly prepared cobalt (II) chloride salt (0.952 g; 4 m mole) and maleic acid (0.464 g; 4 m mole) were mixed in 100 ml of absolute ethanol and reflexed on a water bath for an hour and then the calculated amount of an alcoholic solution of heteroamine bases was added (e.g. 8 m mole of Q, IQ and 4 m mole of 2apy, 8-HQ). The mixture was again reflexed for an hour and then cooled.

At last the solution of the complex 4 was prepared in one equivalent of alcoholic potassium hydroxide. The precipitate formed were filtered, washed several time with ethanol and then dried in a vacuo over phosphorus pentoxide (P_2O_5).

Preparation of the Fe(III) complexes

An ethanolic solution (Just dissolved) of Fe(III) chloride (0.540 g; 2 m mole) and ethanolic potassium hydroxide solution (Just dissolve) of maleic acid (0.464 g; 4 m mole) were mixed in the calculated ratio with constant stirring for ½ h. No precipitates was observed, after which heteroamine bases (4 m mole of Py, 4-pico) wase added with constant stirring for an hour. Precipitate appeared were filtered, washed several times with alcohol and then dried in a vacuum desiccator over phosphorus pentaoxide (P_2O_5).

Anti-microbial test

Fourteen pathogenic bacteria viz ***Staphylococcus aureus*** (Gram positive), ***Streptococcus-β-haemolyticus*** (Gram positive), ***Bacillus megterium*** (Gram positive), ***Bacillus subtilis*** (Gram positive), ***Sarcina lutea*** (Gram positive), ***Salmonella typhi*** (Gram negative), ***Shigella dyscntriae*** (Gram negative), ***Shigella boydii*** (Gram negative), ***Shigella flexneri*** (Gram negative), ***Shigella sonnei*** (Gram negative), ***Shigella shiga*** (Gram negative), ***Klebsiella*** sp. (Gram negative), ***Pseudomonas aerugionsa*** (Gram negative) and ***Escherichia coli*** (Gram negative) and fourteen fungi viz ***Fusarium*** sp., ***Tricophyton*** sp., ***Penicillium*** sp., ***Mucor*** sp., ***Aspergillus flavus***, ***Aspergillus tarreas***, ***Aspergillus vercicolar***, ***Aspergillus niger***, ***Aspergillus nidulans***, ***Candida albicans***, ***Trichoderma vivrudae***, ***Colletotrichum falcatum***, ***Bipolaris sorokiniana*** and ***Sclerotium rolfsii*** were collected from the Department of Pharmacy and Department of botany, University of Rajshahi, respectively and selected for anti-microbial test. The test were performed in plant pathology laboratory Department of Botany, University of Rajshahi. Nutrient agar and potato dextrose agar were used as bacteriological and fungicidal media, respectively. The complexes were dissolved separately in dimethyl sulfoxide (DMSO) to get a concentration of 200 µg disc^{-1}. Then ***in vitro*** anti-microbial activity of these complexes was carried out by disc diffusion method(Bauer ***et al.***, 1966). The diameter of the zone of inhibition produced by the complexes were compared with Kanamycin (30 µg disc^{-1}) and Fluconazol (200 µg disc^{-1}) for bacteria and fungi, respectively.

Results and Discussion

The complexes were characterized on the basis of elementary analysis, melting point and conductance magnetic measurement, infrared and electronic spectra (Table 1). The infrared spectra of the complexes confirmed the coordination of metal with ligands. The presence of water molecule (5) inside the co-ordination sphere was also confirmed by infrared spectra. The magnetic measurements indicated that the Co(II) complexes (1-4) are paramagnetic and show magnetic moment between 3.88 - 4.10 B.M. The electronic spectra of these complexes gave two intense bands at 23940 - 24500 and 29865 - 30060 cm^{-1} corresponding to the transition $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ (v_3) and charge transfer band respectively. For Fe(III) complexes (5-6) the values of magnetic moment lies between 5.68 - 5.87 B.M. The electronic spectra of these complexes gave four bands in the range 18510 - 18745, 21050 - 21195, 24345 - 24785, 25680 - 25775 cm^{-1} corresponding to the transitions $^6A_{1g} \rightarrow {}^4T_{1g}(G)$, $^6A_{1g} \rightarrow {}^4T_{2g}(G)$, $^6A_{1g} \rightarrow {}^4E_g(G)$, $^6A_{1g} \rightarrow {}^4A_{1g}(G)$, respectively. Electronic spectra and magnetic measurement confirmed the tetrahedral (Islam ***et al.***, 1986) and octahedral (Narvi ***et al.***, 1984) structure of Co(II) and Fe(III) complexes, respectively.

Antibacterial activities of these complex compounds were studied and result were presented in Table 2. The highest zone of inhibition were measured respectively 32, 33 and 37 mm against

Table 1: Analytical data and physical properties of the complexes

Complex no.	Complexes	Color	Metal(%)	M.P ordec.temp (±5°C)	Molar conductance ($Ohm^{-1}cm^2mole^{-1}$)	Magnetic moment (B.M)
1	[Co(II)(ME)(2apy)]	Violet	22.06(22.20)	290	16.34	3.95
2	[Co(II)(ME)$(Q)_2$]	Light Blue	13.66(13.86)	200	22.80	4.10
3	[Co(II)(ME)$(IQ)_2$]	Light Blue	13.66(13.88)	190	20.95	4.05
4	K[Co(II)(ME)(8-HQ)]	Thal chocolate	16.56(16.80)	295	68.59	3.88
5	K[Co(II)(ME)(py)H_2O]	Cream	13.29(13.38)	250D	65.38	5.68
6	K[Co(II)(ME)(4-pico)]	Cream	10.96(10.80)	260D	67.89	5.87

M.P= Melting point, dec. temp.= Decomposition temperature, D = Decomposition point, ME = Deprotonated maleic acid

Table 2: Results of the antibacterial activity of the complexes

	Diameter of inhibition zone of bacteria in different complexes* (mm)						
Name of the bacteria	1	2	3	4	5	6	Kanamycin 30 µg/disc
Staphylococcus aureus (+ve)	22	20	24	26	0	0	22
Streptococcus-β-haemolyticus(+ve)	14	32	33	37	8	10	18
Bacillus megaterium (+ve)	14	20	20	28	0	0	25
Bacillus subtilis (+ve)	16	10	16	20	8	8	24
Sarcina lutea (+ve)	8	10	16	26	7	9	23
Salmonella typhi (-ve)	22	10	12	20	6	0	19
Shigella dysenteriae (-ve)	0	16	20	40	0	0	20
Shigella boydii (-ve)	18	16	16	32	0	0	24
Shigella flexneri (-ve)	18	16	16	32	8	9	18
Shigella sonnei (-ve)	20	22	20	34	10	8	23
Shigella shiga (-ve)	8	10	16	28	8	7	26
Klebsiella sp. (-ve)	20	20	12	26	0	0	21
Psudomonas aeruginosa (-ve)	22	22	20	36	10	8	20
Escherichia coli (-ve)	0	10	12	16	0	0	20

Table 3: Results of the antifungal activity of the complexes

		Diameter of inhibition zone of fungi in different complexes* (mm)						
Fungi code	Name of the fungi	1	2	3	4	5	6	Fluconazol
A002	*Fusarium* sp.	14	0	10	12	12	12	15
B002	*Trichophyton* sp.	0	7	0	44	0	8	0
C002	*Penicillium* sp.	0	7	8	12	0	0	22
D002	*Mucor* sp.	24	0	8	12	0	0	0
E002	*Aspergillus flavus*	18	0	0	0	14	0	22
F002	*Aspergillus terreas*	0	0	10	0	0	0	10
G002	*Aspergillus versicolar*	12	0	0	0	14	16	0
H002	*Aspergillus niger*	0	0	0	0	0	0	22
I002	*Aspergillus nidulans*	8	7	8	8	0	13	18
J002	*Candida albicans*	0	0	0	0	0	0	0
K002	*Trichoderma virude*	0	0	0	8	0	0	16
L002	*Colletotrichum falcatum*	0	0	0	0	0	0	35
M002	*Bipolaris sorokiniana*	22	0	0	26	0	8	18
N002	*Sclerotium rolfsii*	10	8	0	10	0	7	28

* Complexes name; see Table 1

streptococcus-β-haemolyticus. No inhibitions zone was found in ***S. aureus***, ***B. bagaterium***, ***S. dysenteriae***, ***S. boydii*** and ***escherichie coli*** when these organisms were treated with the complex no. 1, 5 and 6 respectively. In the other case the complex were should intermediary inhibition zone. It is revealed from the Table 2 that the complex no. 4 has most and complex no. 6 has less antibacterial effect.

In the case of antifungal activities test the highest zone of inhibition 44 and 26 mm of ***Trichophyton*** sp and ***Bipolaris sorokaniana*** respectively were measured in complex no. 4 (Table 3). While rest of the complex have more or less intermediary anti fungal effect against the test fungi. ***Aspergillus nidulans***, ***candida albicans*** and ***Colletotrichum falcatum*** no zones of inhibition were formed in all the tested complexes.

References

Baranyi, A. and O. Feher, 1979. Convulsive effects of 3-aminopyridine on cortical neurones. Electroencephalogr. Clin. Newrophysiol., 47: 745.

Bauer, A.W., W.M.M. Kirby, J.C. Shesies and M. Turck, 1966. Modified ultrafiltration method for detg.serum protein binding and its application to penicillins. Am. J. Clin. Pathol., 44: 93-496

Dell, B.O., 1980. Diodoquin therapy of zinc deficiency in rats. Am. J. Clin. Nutr., 33: 2223

Islam, M.S., 1986. Characterization of mixed ligand complexes of Co(II) and Ni(II) with diphenicacid as a primary and heterocyclic bases as a secondary ligands. synth, React. Inorg. Met-org Chem., 16: 553

Islam, M.S., M.A. Farroque, M.A.K. Bodruddoza, M.A. Mosaddik and M.S. Alam, 2000. Antimicrobial and toxicological studies of mixed ligand transition metal conplexes of schiff bases Bio. Sci., 2: 797-799.

Khadikar, P.V., R. Saxena, T. Khaddar and M.A. Feraqui, 1994. Salicylhydroxamic acid and their metal chelate as antifungal agents, J. India Chem. Soc., 56: 215.

Kulieve, A.M., M.A. Shakhgel, M.A. Gadzheira and I.A. Aliev, 1979b. Electro chemical oxidation of aniline derivatives. Mickroog. Nizshie Rast. Razrishiteli Mater. Izdelli, pp: 150.

Mayer, J., M. Rohn, Puschnan and Mycosen, 1980. Experimental studies on the antimicrobial and antimycotic effects of a preparation containing nystatin and chlorquinald of compared with similar antimicrobial agents, 23: 320.

Nakazawa, S. and T. Yamauchi, 1980. hydroxyquinoline copper and cuprus de as antifouling agent.jnp. Kokai Tokkyo Kohojp; 8051007(CLAON 55/04).

Narvi, S.S., 1984. Ph.D. Thesis, University of Roorkee, Rooekee-247667(India).

Paajnar, L., K. Kaskela and P. Viitaniemi, 1999. Treatment of wood with a mixture of tall oil and maleic anhydride, VTT. Julk, 836: 75.

Part, W.B and W. Ruddon, 1989.The anticancer drugs, pp: 251-254.

Sangal, S.K. and K. Herjinider, 1994. Structure and fungicidal studies of thiazoline metal complexes. J. Indian Chem., 71: 621-623.

Szente, M., O. feher and T. Gyuris, 1984. The effect of aminopyridine on the critical evoked potentials. Acta Physiol. Hung., 63: 197.

Zakaria, C.M., A. Farroque, M.R. Islam and M.H. Biswas, 2000. Antimicrobial screening of ferrocena derivatives of compounds. Oriental J. Chem., 16: 85-90.