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

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Abstract: Mixed-ligand transition metal complexes of Co(II) ions were synthesized, where, Malonic acid 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 had been done. Their anti-bacterial and anti-fungal activity had been evaluated. Disc diffusion methods were employed for anti-microbial assays against fourteen pathogenic bacteria (five gram positive and nine gram negative) and fourteen fungi. The complexes containing 8-hyroxy-quinonline as secondary ligand were much more microbial activity than the other complexes. In addition, the complexes K[Co(II)(MO)(8-HQ)] shows the highest anti bacterial activity against all bacterial tasted (when, MO = $C_3H_2O_4$ and 8-HQ = (C_9H_6NO).

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

Introduction

An exhaustive survey of the existing literature reveals that a very little has been done on the metal complexes of dibasic acid. Malonate complexes are known which Cu (II) metal ion and have been reviewed (Krkishnamurty *et al.,* 1983), complexes formation between iron (III) and oxalate, malonate, succinate and gluterate ion have been studied (Demeux *et al.,* 1968). Synthesized the benzo thiazale ligand and anti-fungal activities have been evaluated (Tiwai *et al.,* 1994). Ni (II), Co (II), Fe (III) and Cu (II) complexes with thiazoline and their fungicizal activity have been evaluated (Kaur, 1994). All of tested 49 strains of fungi were reduced 2.3.5 triphenyl tetrazolium chlorid (T.T.C.) have been reported. But when malonic acid and iodoactic acid were used as inhibitions of endogenous substrate respiration only 50% of Strains (Bhatia *et al.,* 1993). Heterocyclic bases have a great important in biological and industrial fields. Most of the heterocyclic bases are used as corrosion inhibitors as an anti-bacterial, anti-convulsive, anti-fungal and anti-fouling agents. The chlorinated species of 8-hydroxyquinoline has been proved as anti-bacterial and anti-fungal agents and the diiodo derivative is administrated to overcome Zn deficiency in animals (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 3-Aminopyridine has strong anti-conclusive effects (Baranyi *et al.*, 1979; Szente *et al.,*1984). Some mixed ligands complexes of Co (II) and Fe (III) ions with malonic acid (MOH_2) as primary and heterocyclic bases viz. quinoline (Q), iso quinoline (IQ), 8-hydroxyquinoline (8-HQ), pyridine (py), 2-aminopyridine (2apy) and 2-aminophenol (2aph) as secondary ligands have been prepared and their antimicrobial 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 malonic acid (0.416 g; 4 m mole) were mixed in 100 ml of absolute ethanol and refluxed on a water bath for an hour and then the calculated amount of an alcholoic solution of heteroamine bases was added (e.g. 8 m mole of Py, Q, IQ and 4 m mole of 2apy, 2aph, 8-HQ). The mixture was again refluxed for an hour and then cooled.

At last the solution of the complexes (only 5 and 6) was prepared in one equivalent of alcoholic KOH. The precipitate formed were filtered, washed several times with ethanol and then dried in 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 malonic acid (0.416 g; 4 m mole) were mixed in the calculated ratio with constant stirring for 30 min. No precipitates was observed after which heteroamine bases (Q, IQ = 0.576 g; 4 m mole) was added with constant stirring for an hour. At last the solution of complexes was prepared in one equivalent of alcoholic potassium hydroxide. The precipitate appeared were filtered, washed several times with alcohol and then dried in a vacuum desiccator over phosphorus pentioxide (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., *Tricopyton* sp., *Penicillium* sp., *Mucor* sp., *Aspergillus flavus, Aspergillus tarreas, Aspergillus vercicolar, Aspergillus niger, Aspergillus nidulans, Candida albicans, Trichoderma vivruade, Collectotrichum falcatum, Bipolaris sorokiniana* and *Sclerotium rolfsii* were collected from 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. The diameter of the zone of inhabitation produced by the complexes was 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 ion with ligands. The magnetic measurements indicated that the Co (III) complexes (1-6) are paramagnetic and show magnetic moment 3.91-4.21 B.M. The electronic spectra of these complexes gave two intense bands at 24,000-24,500 cm^{-1} and 30,000-30,154 cm^{-1} corresponding to the transition $^4A_{2g}$ (F)→$^4T_{1g}$ (P) (V_3) and charge transfer band respectively. For Fe (III) complexes (7-8) the values of magnetic moment lies between 6.00-6.20 B.M. The electronic spectra of these complexes gave four bands in the range 18500-18725, 21000-21185, 24325-24750 and 25770-25640 cm^{-1} corresponding to the transitions $^6A_{1g}$→ $^4T_{1g}$ (G), $^6A_{1g}$ → $^4T_{2g}$ (G),^{6} A_{1g} → $^4A_{1g}$→ $^4A_{1g}$ (G) respectively. The Co (II) complexes are assumed to have tetrahedral (Islam, 1986)

Table 1: Analytical data and physical properties of the complexes

Complex no.	Complexes	Color	Metal (%)	M.P. or dec. temp (±5°C)	Molar conductance (Ohm^{-1}cm^2 mole^{-1})	Magnetic moment (B.M.)
1	[Co(II)(MO)(py)$_2$]	Purple	18.46 (18.41)	255D	16.29	4.05
2	[Co(II)(MO)(2apy)]	Light purple	23.10 (23.04)	260D	14.31	4.21
3	[Co(II)(MO)(Q)$_2$]	Blue	14.05 (13.90)	245	19.50	4.10
4	[Co(II)(MO)(IQ)$_2$]	Light blue	14.05 (13.85)	240	20.45	3.98
5	K[Co(II)(MO)(8-HQ)]	Light blue	14.47 (14.49)	290D	68.38	3.91
6	K[Co(II)(MO)(2aph)]	Thal chocolate	15.88 (15.90)	210	62.52	3.95
7	K[Co(II)(MO)$_2$(Q)$_2$]	Cream	9.00 (9.03)	185	63.15	6.00
8	K[Co(II)(MO)$_2$(IQ)$_2$]	Cram	9.00 (9.05)	183	72.64	6.20

M.P. = Melting point, dec. temp. = Decomposition temperature, D = Decomposition point MO = Deprotonated malonic acid.

Table 2: Results of the antibacterial activity of the complexes

		Diameter of inhibition zone of bacteria in different complexes (mm)*								
Bacteria code	Name of bacteria	1	2	3	4	5	6	7	8	Kanamycin 30 μg disc^{-1}
A001	*Staphylococcus aureus* (+ve)	0	20	0	0	22	20	8	0	22
B001	*Staphylococcus-β-haemolyticus* (+ve)	8	15	0	0	22	14	0	8	18
C001	*Bacillus megaterium* (+ve)	15	20	28	20	28	16	12	13	25
D001	*Bacillus subtilis* (+ve)	8	12	14	8	16	16	10	8	24
E001	*Sarcina lutea* (+ve)	8	32	16	14	38	10	10	10	23
F001	*Salmonella typhi* (-ve)	12	18	16	14	30	14	13	12	19
G001	*Shigella dysenteriae* (-ve)	17	33	16	16	40	10	10	10	20
H001	*Shigella boydii* (-ve)	22	26	20	24	30	12	0	0	24
I001	*Shigella flexneri* (-ve)	13	31	12	16	36	18	10	12	18
J001	*Shigella sonnei* (-ve)	15	10	16	14	32	10	10	12	23
K001	*Shigella shiga* (-ve)	8	12	20	22	24	30	10	8	26
L001	*Klebsiella* sp.(-ve)	0	9	20	10	22	8	10	0	21
M001	*Psudomonas aeruginosa* (-ve)	8	18	12	14	26	10	10	10	20
N001	*Escherichia coli* (-ve)	10	15	10	8	20	8	10	10	20

* Complexes name see Table 1

Table 3: Results of the antifungal activity of the complexes

Fungi code	Name of fungi	Diameter of inhibition zone of bacteria in different complexes (mm)* 1	2	3	4	5	6	7	8	Fluconazol
A002	*Fusarium* sp.	0	7	0	0	12	0	0	0	15
B002	*Trichophyton* sp.	7	0	8	0	32	0	8	0	0
C002	*Penicillium* sp.	0	8	0	0	10	0	0	0	22
D002	*Mucor* sp.	0	8	0	0	8	0	0	0	0
E002	*Aspergillus flavus*	0	10	0	0	8	0	0	8	22
F002	*Aspergillus terreas*	0	8	7	0	8	8	0	0	10
G002	*Aspergillus versicolar*	8	8	0	8	10	0	7	8	0
H002	*Aspergillus niger*	0	0	0	0	0	0	0	0	22
I002	*Aspergillus nidulans*	8	8	0	0	12	0	0	8	18
J002	*Candida albicans*	0	0	0	0	0	0	0	0	0
K002	*Trichoderma virude*	8	8	0	10	12	8	0	6	16
L002	*Colletotrichum falcatum*	0	0	0	0	0	0	0	0	35
M002	*Bipolaris sorokiniana*	0	8	8	8	34	10	8	0	18
N002	*Sclerotium rolfsii*	0	0	0	0	12	0	0	6	28

* Complexes name see Table 1

and the Fe (III) complexes have octahedral structures based on the electronic spectra and magnetic measurement.

Anti-bacterial activity of these complex compounds were studied and result were presented in Table 2. The highest zone of inhibition 22, 33, 28, 22, 40, 30, 13 and 13 mm were measured in *S. boydii S. dysenteriae, B. megaterium, S. shiga, S. dysenteriae, S. shiga, S. typhi* and *B. megaterium* respectively. No inhibition zone was found in *S. aureus, Stroptcoccus-ß-haemolytices, S. boydii, Klebsiella* sp. when these organisms were treated with the complex were showed intermediary inhibition zone. It is revealed from other cases the complex no. 5 has most and complex no. 7 has less anti-bacterial effect.

In the case of antifungal activities test the highest zone of inhibition 32 and 34 mm of *Trichophyton* sp and Bipolaris sorokiniana respectively were measured in complex no. 5. While rest of the complexes have more or less intermediary anti-fungal effect against the tested fungi. *Aspergillus nidulans, Candida albicans* and *Colletotrichum falcatum.* No zone of inhibition were found in all the tested complexes (Table 3).

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