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# Antimicrobial Studies of Mixed Ligand Transition Metal Complexes of Phthalicacid and Heterocyclicamine Bases

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**Abstract:** Mixed-ligand transition metal complexes of Pt (IV) ions were synthesized, where, Phthalic acid as a primary ligands and heterocylicamine bases as a secondary ligands have been used, respectively. Moreover, mixed-ligand transition metal complexes of Ni (II) ions were also synthesized by the same way, which, mentioned before except Ni(II)ions used instead of Pt (IV) ions. 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-hyroxyquinoline as secondary ligand were much more microbial active than the other complexes. In addition, the complexes; $[Pt(IV)(PA)(8\text{-}HQ)_2]$ shows the highest anti-bacterial activity against all bacteria tested (When, PA = $C_8H_4O_4$ and 8-HQ = $C_9H_6NO$)

**Key words:** Biological activity, phthalicacid, heterocylicamine bases mixed-ligands complexes

## Introduction

Most of the insecticides, in their early stage of the inorganic compounds having bad odor and are very ugly to look at (Haque, 1991). The production of effective poisons in that regards, since from the middle of 19th century. The arsenate compound of Ca, Pb, S and Paris green $[Cu(C_2H_3O_2)_2.\ 3Cu(AsO_2)]$ were remarkable among them.

The complexes of platinum metal are very important from medicinal point of view. Some complexes of platinum exhibit anti-tumor activity (Harder *et al*., 1970) and leukemia's (Welsch, 1971). On the other hand, Ni(II), Co(II), Fe(III) and Cu(II) complexes with thiazoline and their fungicidal activity have been evaluated (Kaur, 1994). The metal complexes of phthalicacid have been studied both from pharmacological and industrial (Nippon Synthetic Chemical Industry Co. Ltd.) point of view as indicated by available literature. In addition, heterocyclic bases have a great important in biological and industrial fields. Most of the heterocyclic bases are used as corrosion inhibitors and as 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 (Mayer *et al*., 1980) and the di iodo derivative is administrated to overcome Zn deficiency in animals (Dell, 1980). Derivatives of Cu with 8-hydroxyquinoline are antifouling agent (Nakazawa *et al*., 1980) and itself protects the industrial and fungi in them (Kulieve *et al*., 1979a,b). 3-Aminopyridine has strong anti-convulsive effects (Baranyi and Feher, 1979; Szente *et al*., 1984). Therefore, some mixed ligand complexes of Pt (IV) and Ni (II)ion with phthalicacid ($PAH_2$) as primary and heterocyclic bases, viz., quinoline(Q), Iso-quinoline(IQ), pyridine (Py), 2-aminopyridine (2apy), 8-hydroxyquinoline (8-HQ), as secondary ligands have been prepared and their anti-microbial studies have been carried out to perform for primary selection of these complexes as the therapeutic agents.

## Materials and Methods

**General methods of complexes preparation:** A 25 ml of ethanolic solution of the metal salt ($PtH_2Cl_6$/$NiCl_2.6H_2O$) (1 m mole) and phthalicacid (2 m mole for complexes 1-4 and 1 m mole for complexes 5-8) were mixed in the calculated ratio with constant stirring. No precipitate was observed. Then 25 ml of an ethanolic solution of heterocyclicamine bases (e.g. 2 m mole of Py, Q, IQ, 8-HQ and 1 m mole of 2apy) was added to the resulting hot plate with constant stirring. The volume of the solution was reduced to an half and allowed to cool. The precipitate formed and were filtered, washed several time with ethanol and then dried in dedicator over anhydrous $CaCl_2$.

**Anti-microbial test:** Fourteen pathogenic bacteria (five gram positive and nine gram negative) and fourteen fungi were collected from Department of Pharmacy and Department of Botany, University of Rajshahi respectively and selected for anti-microbial test. The tests 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 the disc diffusion method (Bauer *et al*.,1966). The diameter of the zone of inhibition produced by the complexes was compared with Kanamycin (30 μg $disc^{-1}$) and Fluconazol (200 μg $disc^{-1}$) for bacteria and fungi, respectively.

Statistical analysis of data given as percentage was carried out from angular transformed values and performed using Microsoft Excel software. LSD were determined, whenever, the calculated 'F' values were significant at 5% level (Snedecor and Cochran, 1980).

## Results and Discussion

The complexes were characterized on the basis of elementary analysis, melting point, conductance, magnetic measurement, infrared and electronic spectra (Table 1). The infrared spectra of the complexes confirmed the coordination of metal ion with ligands. The presence of water molecule (7, 8) inside the co-ordination sphere was also confirmed by infrared spectra. The observed magnetic moment values of Pt (IV) complexes (1-5) indicated that these complexes are diamagnetic. This diamagnetism is supported by small values obtained for their magnetic susceptibility. For Ni (II) complexes (6-8) the values of magnetic moment lies between 2.76-2.79 B.M. The electronic spectra of Ni (II) complexes gave the bands at 14005-14505 $cm^{-1}$ corresponding to the transition $^3T_1(F) \rightarrow {}^3T_1(P)$. Electronic spectra and magnetic measurement confirmed that the Pt (IV) complexes were of octahedral and the Ni (II) complexes were of tetrahedral (Islam, 1986) structure.

Antibacterial activities of these complex compounds were studied and results were presented in Table 2. The highest zone of inhibition 36, 28, 25, 26, 123, 28, 22 and 22 mm were measured in *Staphylococcus aureus, Bacillus megaterium, Shigella shiga, S. sonnei, S. flexneri, B. megaterium, S. shiga* and *Psudomonas aeruginosa* respectively (Table 2).In this experiment, in case of complex no. the lowest inhibition zone were measured respectively 8, 16 and 15 mm in *Escheria coli.* Complex no. 4 and 8 show the lowest inhibition zone 16 and 8 mm respectively against *Shigella dysenteriae*. In case of complex no. 5, 6 and 7, the lowest inhibition zone were measured 54, 6 and 9 mm in *B. megaterium, Streptococcus-β-haemolyti*cus and *Klebsiella* sp. respectively. were found in complex no. 1 and 5 respectively. No inhibition zone was found in *S. aureus, S. boydii* and *Escheria coli* when these organisms were treated with the complex no. 2 and 6, 3 and 4, 7 and 8 respectively. In other cases the complexes were showed intermediary inhibition zone. It is revealed from the Table 2 that the complex no. 5 has most and the

Table 1: Analytical data and physical properties of the complexes

| Complex no. | Complexes | Color | Metal(%) | M.P or dec.temp (±5°C) | Molar conductance ($Ohm^{-1}cm^2mole^{-1}$) | Magnetic Moment (B.M) |
|---|---|---|---|---|---|---|
| 1 | $[Pt(IV)(PA)_2(py)_2]$ | Cream | 28.62(28.58) | 245 | 10.55 | Diam |
| 2 | $[Pt(IV)(PA)_2(2apy)]$ | Yellow | 31.60(31.56) | 250 | 11.20 | Diam |
| 3 | $[Pt(IV)(PA)_2(Q)_2]$ | Cream | 24.96(24.92) | 240 | 12.90 | Diam |
| 4 | $[Pt(IV)(PA)_2(IQ)_2]$ | Cream | 24.96(24.91) | 240 | 12.85 | Diam |
| 5 | $[Pt(IV)(PA)(8\text{-}HQ)_2]$ | Yellow | 30.13(30.15) | 250 | 14.80 | Diam |
| 6 | $[Ni(II)(PA)(py)_2]$ | Light alpine | 15.40(15.43) | 248D | 19.90 | 2.78 |
| 7 | $[Ni(II)(PA)(Q)(H_2O)]$ | Alpine | 15.86(15.82) | 258D | 11.62 | 2.76 |
| 8 | $[Ni(II)(PA)(IQ)(H_2O)]$ | Alpine | 15.86(15,81) | 260D | 11.76 | 2.79 |

M.P- Melting point, dec. temp.- Decomposition temperature, D-Decomposition point, Diam- Diamagnetic, PA-Deprotonated Phthalic acid

Table 2: Results of the antibacterial activity of the complexes

| | | Diameter of inhibition zone of bacteria in different complexes[1] (mm) | | | | | | | | Calculated 'F' | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bacteria code | Name of the bacteria | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Bacteria | Inhibition zone | $LSD_{(0.05)}$ |
| A001 | *Staphylococcus aureus* (+ve) | 36 | 0 | 20 | 22 | 102 | 0 | 20 | 18 | 66.9264* | 6234.602* | 3.37229 |
| B001 | *Strptococcus-β-haemolyticus*(+ve) | 26 | 25 | 18 | 17 | 100 | 6 | 14 | 16 | | | |
| C001 | *Bacillus megaterium* (+ve) | 24 | 28 | 20 | 20 | 54 | 28 | 16 | 14 | | | |
| D001 | *Bacillus subtilis* (+ve) | 22 | 18 | 20 | 18 | 60 | 14 | 10 | 12 | | | |
| E001 | *Sarcina lutea* (+ve) | 18 | 20 | 18 | 20 | 86 | 10 | 16 | 17 | | | |
| F001 | *Salmonella typhi* (-ve) | 32 | 21 | 24 | 22 | 86 | 16 | 17 | 15 | | | |
| G001 | *Shigella dysenteriae* (-ve) | 16 | 26 | 26 | 16 | 104 | 17 | 10 | 8 | | | |
| H001 | *Shigella boydii* (-ve) | 29 | 17 | 0 | 0 | 101 | 20 | 16 | 15 | | | |
| I001 | *Shigella flexneri* (-ve) | 20 | 23 | 21 | 20 | 120 | 12 | 12 | 12 | | | |
| J001 | *Shigella sonnei* (-ve) | 24 | 24 | 24 | 26 | 100 | 16 | 20 | 20 | | | |
| K001 | *Shigella shiga* (-ve) | 24 | 21 | 25 | 24 | 94 | 21 | 22 | 19 | | | |
| L001 | *Klebsiella* sp. (-ve) | 18 | 21 | 20 | 19 | 63 | 20 | 9 | 9 | | | |
| M001 | *Psudomonas aeruginosa* (-ve) | 28 | 17 | 21 | 20 | 96 | 12 | 18 | 20 | | | |
| N001 | *Escherichia coli* (-ve) | 8 | 16 | 15 | 23 | 90 | 10 | 0 | 0 | | | |

[1]Complexes name see table-1, *Significant at 5% level probability

Table 3: Results of the antifungal activity of the complexes

| | | Diameter of inhibition zone of fungi in different complexes[1] (mm) | | | | | | | | Calculated 'F' | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fungi code | Name of the fungi | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Fungi | Inhibition zone | $LSD_{(0.05)}$ |
| A002 | *Fusarium* sp. | 12 | 18 | 10 | 14 | 24 | 7 | 8 | 10 | 751.2497* | 856.5845* | 1.80196 |
| B002 | *Trichophyton* sp. | 0 | 1 | 8 | 10 | 54 | 0 | 16 | 14 | | | |
| C002 | *Penicillium* sp. | 0 | 0 | 0 | 0 | 10 | 0 | 16 | 14 | | | |
| D002 | *Mucor* sp. | 0 | 8 | 0 | 0 | 10 | 0 | 0 | 0 | | | |
| E002 | *Aspergillus flavus* | 0 | 18 | 10 | 10 | 20 | 8 | 0 | 0 | | | |
| F002 | *Aspergillus terreas* | 0 | 0 | 0 | 0 | 8 | 0 | 16 | 14 | | | |
| G002 | *Aspergillus versicolar* | 0 | 8 | 0 | 0 | 8 | 0 | 18 | 16 | | | |
| H002 | *Aspergillus niger* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| I002 | *Aspergillus nidulans* | 10 | 8 | 0 | 0 | 18 | 0 | 16 | 14 | | | |
| J002 | *Candida albicans* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| K002 | *Trichoderma virude* | 0 | 0 | 24 | 22 | 36 | 0 | 0 | 0 | | | |
| L002 | *Colletotrichum falcatum* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| M002 | *Bipolaris sorokiniana* | 14 | 18 | 18 | 16 | 44 | 8 | 34 | 32 | | | |
| N002 | *Sclerotium rolfsii* | 10 | 0 | 0 | 0 | 16 | 0 | 16 | 14 | | | |

[1] Complexes name see table-1, * Significant at 5% level of probability

complex no. 8 has less antibacterial effect. Analysis of variance showed that the inhibition effects of the complexes on the bacterial growth are significantly different. LSD value also same results.

In the case of antifungal activities test, the highest zone of inhibition 24, 54, 10, 20, 18, 36 and 44 mm of *Fusarium* sp. *Mucor* sp. *Aspergillus flavus, A. nidulans, Trichoderma virude* and *Bipolaris sokiniana* respectively were measured in complex no. 5. In case of *Penicillium* sp., *A. terreas, A. versicolar* and *Sclerotium rolfsii* the highest inhibition zone 16, 16, 18 and 18 mm respectively were found in complex no. 7. The lowest inhibition zone 7 and 8 mm in *Fusarium* sp. and *S. rolfsii* respectively were measured in complex no. 6. Inhibition zone of *Trichophyton* sp. in complex no. 1 and 6, *Penicillium* sp. in complex no. 1, 2, 3, 4 and 6, *Mucor* sp. in complex no. 1, 3, 4, 6, 7 and 8, *A. flavus* in complex no. 1, 7 and 8, *A. terreas* in complex no. 1, 2, 3, 4 and 6, *A. versicolar* in complex no. 1, 3, 4 and 6, *A. nidulans* in complex no. 3, 4 and 6, *T. virude* in complex no. 1, 2, 6, 7 and 8 and *S. rolfsii* in complex no. 2, 3, 4 and 6 were no found. In case of *A. niger, Candida albicans* and *Colletotrichum falcatum* no zone of inhibition were formed in all the tested complexes. Analysis of variance showed that the inhibition effects of the complexes on the mycelial growth of fungi are significantly different. LSD value also same results.

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