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Research Article

Study of Biological Activity of Mixed Ligand of some 3d Metal Complexes against Clinically Microbial Isolates

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ABSTRACT:

Mixed ligand complexes consisting of Cobalt (II), Nickel (II), and Copper (II) ions along with phthalimide and heterocyclic amines have found extensive applications in biological, industrial, and analytical fields. These complexes namely [Cu(II)(Ph-imide)$_2$(Py)$_2$], [Co(II)(Ph-imide)$_2$(Py)$_4$] and [Ni(II)(Ph-imide)$_2$(Py)$_4$], where Ph-imide = Phthalimide and Py = Pyridine, The unique structural and electronic properties of metal complexes have made them promising candidates for antibacterial therapy. In this study, we assessed the antibacterial activity of these metal complexes against both Gram-positive (*Staphylococcus aureus)* and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa.* and Acinetobacter *spp.*) bacteria. The antibacterial activity was evaluated using the cup-plate diffusion method and compared to that of standard antibiotics. The results showed that the metal complexes exhibited moderate to high antibacterial activity against both types of bacteria with some complexes even demonstrating superior activity compared to the standard antibiotics. Furthermore, the observed antibacterial activity was influenced by the specific metal ion and the structure of the ligands used.

Keywords: Antimicrobial activity, metal complexes, ligand.

1. Introduction:

An antimicrobial agent refers to any chemical or biological substance that can either kill microorganisms or inhibit their growth. Antibacterial testing of metal complexes is an important step in the development of new antimicrobial agents. Metal complexes offer several advantages over conventional antibiotics, including their unique structural and electronic properties, which can lead to improved efficacy and reduced toxicity (Claudel,2020 and Sánchez-López, 2020).

Some series of metal complexes containing Copper, Nickel, and Zinc have significant antibacterial activity against various gram-positive and gram-negative bacteria, with some complexes showing higher activity than standard antibiotics such as amoxicillin and ciprofloxacin. The study also highlighted the importance of selecting appropriate bacterial strains for testing, as different strains can exhibit varying levels of susceptibility to metal complexes (Balakrishnan, 2019).

The antibacterial activity of metal complexes containing Cobalt, Copper, and Zinc was also evaluated against gram-positive and gram-negative bacteria. The study demonstrated that the metal complexes exhibited potent antibacterial activity, with some complexes showing MIC values in the nanomolar range. The study also highlighted the potential of metal complexes as effective agents against multidrug-resistant bacteria, which are a major global health concern (HadiKargara, 2021).

Transition metal complexes have proven their significance across various domains of chemistry, making notable contributions to society. One area that has garnered significant attention from medicinal chemists is the antimicrobial applications of metal complexes. This is particularly crucial as pathogenic microorganisms have developed resistance against conventional antibiotics derived from organic compounds. Copper has long been recognized for its antimicrobial and therapeutic properties (Marwah *et al,* 2022; El-Sawaf, *et al*.,2018, and Prasad *et al.*, 2021).

Previously, we studied the antimicrobial activity of a few mixed ligand complexes containing heterocyclic amine as secondary ligands and a few Schiff base-containing complexes. We report here, the antimicrobial activity of new mixed ligand complexes of Co (II), Cu (II), and Ni (II) with Phthaliimides as primary and heterocyclic amine bases as secondary ligands (Li *et al*.,2021).

2. Materials and Methods

2.1 Complexes' synthesis:

Deprotonated amino acid (1 mmole) and metal salt (1 mmole) were combined in an ethanolic solution. Calculated ratio while stirring continuously, but no precipitate was seen. The resulting mixture was then mixed continuously while being heated on a magnetic regulator hotplate with 25 ml of an ethanolic solution of Ligand (4 m mole). Half of the original volume was lost. It was then permitted to cool at room temperature. The precipitate was filtered, washed with ethanol several times, and dried in a desiccator over anhydrous $CaCl_2$ after it had formed.

2.2 Culture media for Clinical bacterial isolates

MacConkey agar, Blood agar, and Chromogenic agar were used for sub-culturing the bacterial isolates; while Klignar-Iron Agar (KIA), MIU, and Simon's citrate agar were used for the identification of bacterial isolates and Muller-Hinton Agar was used for susceptibility test.

2.3 Culture of bacterial isolates

The study utilized culture media to cultivate several bacterial strains namely *Escherichia coli*, *Acinetobacter* spp, *Pseudomonas aeruginosa,* and *Staphylococcus aureus*. Then incubated at 37°C for a duration of 24 hours. The tested organisms were found to pose a risk to human health. All experimental procedures were conducted with utmost care and adherence to aseptic conditions. The research took place in the Department of Microbiology at Khwaja Yunus Ali University, Bangladesh from August 2022 to April 2023.

2.4 Determination of Antibacterial susceptibility testing of mixed ligand by Cup-plate Diffusion Method

The agar cup diffusion method was used to evaluate the antibacterial activity of mixed ligands agains*t* four clinical bacterial strains. Wells or cups of 8 mm diameter were made. Mixed ligand solution was propelled directly into the wells of the inoculated plates, allowed to stand for 10 min for diffusion, and incubated at 37°C for 24 hours. The zone sizes were interpreted as per Clinical Laboratory Standards Institute (CLSI) guidelines. After incubation for 24 hours at 37°C, the plates were observed for antibacterial activity by zone of inhibition. The zone of inhibition was measured using vernier calipers and expressed in millimeters. To avoid any type of contamination by the test organisms the antimicrobial screening was done in laminar air flow and all types of precautions were highly maintained.

3. Results and discussions

The antimicrobial activity of Co(II), Ni(II), and Cu(II) metal complexes was investigated in this study. The results obtained provide valuable insights into the potential of these metal complexes as antimicrobial agents. The study demonstrated that all three metal complexes of Co(II), Ni(II), and Cu(II), exhibited significant antimicrobial activity against a range of bacterial strains. This suggests that these metal complexes possess inherent properties that inhibit the growth and viability of microorganisms.

In particular, the Co(II) metal complex displayed notable antimicrobial activity, effectively inhibiting the growth of both Gram-positive and Gram-negative bacteria. This finding suggests that the Co(II) complex has a broad spectrum of activity, making it a promising candidate for further investigation and potential application in antimicrobial therapies. The resulting data is given in Table:1 and the photo in Figure:1

Table 1: In vitro antibacterial activities of the compound [Co(II)(Ph-imide)$_2$(py)$_4$] complex.

Sl. No.	Bacteria	Gram Staining	Diameter of zone inhibition (in mm)		
			50 µg/disc	100 µg/disc	150 µg/disc
1	*Pseudomonas aeruginosa.*	Negative	10	20	25
2	*Staphylococcus aureus.*	Positive	15	23	31
3	*Escherichia coli*	Negative	15	25	30
4	*Acinetobacter spp.*	Negative	25	35	40

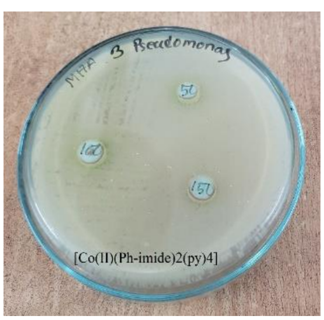

Photo1: Against *Pseudomonas aeruginosa*

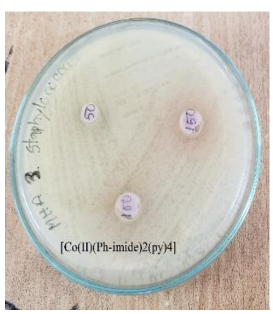

Photo 2: Against *Staphylococcus aureus*

Photo 3: Against *Escherichia coli*

Photo 4: Against *Acinetobacter* spp

Figure 1: Photographic representation of zone of inhibition of the complexes [Co(II)(Ph-imide)$_2$(py)$_4$]

Similarly, the Ni(II) and Cu(II) metal complexes demonstrated considerable antimicrobial potential. These results indicate that the Ni (II) and Cu(II) complexes may have specific mechanisms of action that target and disrupt the cellular processes of microorganisms. The resulting data is given in Tables: 2 and 3 and the photo is in Figures 5 and 6.

Table 2: In vitro antibacterial activities of the compound [Ni(II)(Ph-imide)$_2$(py)$_4$] complex.

Sl. No.	Clinical Bacterial isolates	Gram Staining	Diameter of zone inhibition (in mm)		
			50 µg/disc	100 µg/disc	150 µg/disc
1	*Pseudomonas aeruginosa.*	Negative	0	30	33
2	*Staphylococcus aureus.*	Positive	28	40	45
3	*Escherichia coli*	Negative	0	20	22
4	*Acinetobacter* spp.	Negative	0	20	22

Table 3: In vitro antibacterial activities of the compound [Cu(II)(Ph-imide)$_2$(py)$_2$] complex.

Sl. No.	Clinical Bacterial isolates	Gram Staining	Diameter of zone inhibition (in mm)		
			50 µg/disc	100 µg/disc	150 µg/disc
1	*Pseudomonas aeruginosa*	Negative	20	28	35
2	*Staphylococcus aureus*	Positive	10	18	20
3	*Escherichia coli*	Negative	14	15	16
4	*Acinetobacter spp.*	Negative	12	30	36

Photo 5: Against *Pseudomonas aeruginosa*

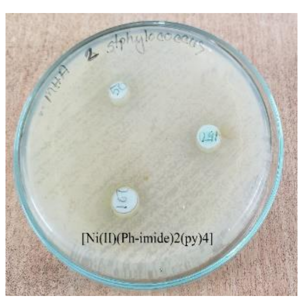

Photo 6: Against *Staphylococcus aureus*

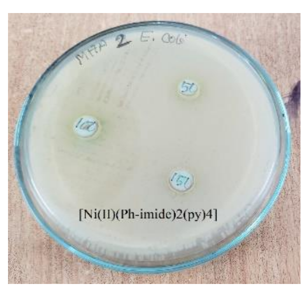

Photo 7: against *Escherichia coli*

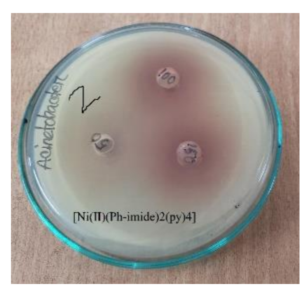

Photo 8: against *Acinetobacter* spp

Figure 2: Photographic representation of zone of inhibition of the complexes [Ni(II)(Ph-imide)$_2$(py)$_4$]

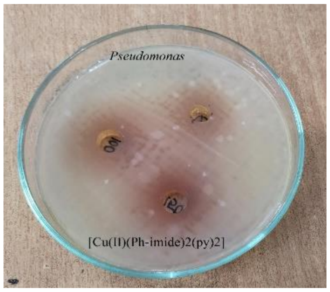

Photo 9: Against *Pseudomonas aeruginosa*

Photo 10: Against *Staphylococcus aureus*

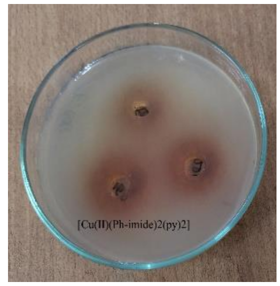

Photo 11: Against *Escherichia coli*

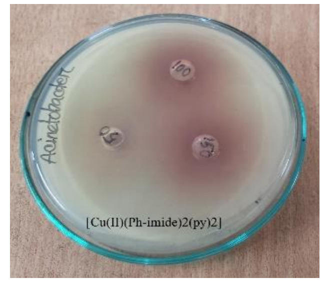

Photo 12: Against *Acinetobacter* spp

Figure 3: Photographic representation of zone of inhibition of the complexes [Cu(II)(Ph-imide)$_2$(py)$_2$]

Overall, the findings of this study suggest that Co(II), Ni(II), and Cu(II) metal complexes possess significant antimicrobial activity against both Gram-positive and Gram-negative bacteria (Table 1,2,3 and photo 1-12). These results support further exploration of these metal complexes for potential therapeutic applications in combating microbial infections.

Escherichia coli is the most susceptible species to all three types of metal complexes, with Co(II) complexes showing the highest antibacterial activity (30 for Co(II), 22 for Cu(II), and 16 for Ni(II)). *Pseudomonas aeruginosa* and *Staphylococcus aureus* are moderately susceptible to all three types of complexes, *Acinetobacter* spp is the least susceptible species to all complexes, with Co(II) complexes displaying the highest antibacterial activity (40). Based on implication for application Co(II) complexes may be the most promising candidates for further development as antibacterial agents due to their consistently high activity across all tested bacterial species.

4. Conclusion:

The information provided suggests that Co(II) mixed ligand complexes have the highest antibacterial properties, followed by Cu(II) mixed ligand complexes with moderate antibacterial properties and Ni(II) mixed ligand complexes with the lowest antibacterial properties. This information can be useful in the development of antibacterial agents and materials as it highlights the potential of using metal-ligand complexes to achieve antibacterial activity. Additionally, the findings suggest that the choice of metal ion and ligand can have a significant impact on the antibacterial properties of the resulting complex.

However, it is important to note that the effectiveness of a complex as an antibacterial agent may also depend on other factors, such as the specific bacterial strain being targeted and the conditions under which the complex is applied. These studies demonstrate the potential of metal complexes as effective antimicrobial agents against both gram-positive and gram-negative bacteria. Therefore, further research may be needed to fully evaluate the potential of these complexes as antibacterial agents.

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7. Authors Contributions
Research concept and Research design - Md. Abul Bashar, Materials & Data collection – Samim Mia, and Abdul Alim, Data analysis and Interpretation- - Md. Abul Bashar and Mohammad Zakerin Abedin, Literature search & Writing article-Md. Abul Bashar, Critical review & Article editing-Mohammad Zakerin Abedin, Final approval- All authors.

8. Disclosure
The authors declare that they have no conflicts of interest in this study.

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