ORIGINAL ARTICLE

Promising Effect of Mixed Ligand Transition Metal Complexes on Antimicrobial Properties

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ABSTRACT:

Metal ion complexes of Co(III), Cu(II), Fe(III), Cr(III) and Ni(III) have positive effect in the development of antimicrobial properties. The ligand and the complexes have been examined for antibacterial activity against a range of Gram-positive (Bacillus authracis, Bacillus cereus, Bacilis subtilis Staphylococcus aureus, Streptococcus agalactiae) and Gram-negative bacteria (Escherichia coli, Shigella dysenteriae, Shigella sonnei). In this present study, we report here the antimicrobial properties of transition metal mixed ligand complexes. Our results are consistent with that of others.

***Key words:** Antibacterial activity, metal complexes, ligand.*

1. Introduction:

Antimicrobial agent indicates any chemical or biological agent that either kills or inhibits the growth of microorganism. The susceptibility of microorganism to antimicrobial agent can be determined in vitro by a number of methods. The disc diffusion technique [1,2] was widely acceptable for preliminary investigation of materials, which were suspected to pose antimicrobial properties. Diffusion procedure was normally used for qualitative test, which allocates organism of the susceptible intermediate (moderately susceptible) or resistant categories.

Many biological processes in living organisms have been affected by metal ions. Metal complexes comprise of a central metal atom surrounded by ligands [3] and produce metal complexes significantly used in treatment of human diseases including cancer, leukemia, infection and inflammation [4]. Recently, works on metal complexes have been reported to deliver drugs to target sites, leading to reduce side effects and improve pharmacokinetics. Metal complexes of 8-hydroxyquinoline (8HQ) have shown to be antiviral, antiparasitic, antioxidant, anti-inflammatory, and anti-diabetic agents [5-7]. Due to metal binding/ chelating abilities and lipophilicities to penetrate cell membranes, Quinoline-based compounds have high selectivity of human malaria [8]. For treatment of rheumatoid arthritis, gold containing complexes are normally used [9]. Sequentially, radiopharmaceuticals based on metals such as technetium and rhenium are used in imaging and radiotherapy [10], and ruthenium complexes have some success as anticancer drugs [11]. The complexes of gadolinium, cobalt, lithium, bismuth, iron, calcium, lanthanum, gallium, tin, arsenic, rhodium, copper, zinc, aluminum and lutetium have significant medicinal property [12]. More recently, cobalt(III) based ligand complexes have been found to possess antiviral and antibacterial activities. We reviewed here the current status of the biological activities of cobalt(III) complexes formed with mono and polydentate ligands.

Previously, we studied antibacterial properties of metal complexes of Co(II) and Fe(III) with tartaric acid or succinic acid and hetero cyclic amines [13-14].

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2. Materials And Methods

The bacterial strains *Escherichia coli, Shegella dysenteriae, Shegella sonnei, Bacillus subtilis, Staphylococcus aureus Bacillus cerus, Streptococcuc agalactiae* were used for this work, cultured in Muller-Hinton Agar medium (Oxoid, UK), and incubated at 37°C for 24 h. The test organisms were pathogenic for human beings. For this reason, all steps of the work were done with high precaution and aseptic conditions which were mentioned below. The tests were carried out at Microbiology Laboratory, Department of Pharmacy, Rajshahi University, Bangladesh during the time duration August 2012 to February 2013.

2.1. Synthesis of complexes:

An ethanolic solution of metal salt (1 mmole) and deprotonated amino acid (1 mmole) were mixed in the calculated ratio with constant stirring but no precipitate was observed. Then 25 ml of an ethanolic solution of L (4 m mole) was added to the resulting mixture and heated on a magnetic regulator hotplate with constant stirring. The volume reduced to one half. After that it was allowed to cool at room temperature. The precipitate formed and were filtered, washed several times with ethanol and then dried in a desiccator over anhydrous $CaCl_2$.

2.2. Antimicrobial screening:

2.2.1. Media used:

Nutrient broth (Oxiod, UK) and Nutrient Agar (Oxoid UK) were used for sub culturing the bacterial isolates, while Muller-Hinton Agar (Oxoid UK) was used for sensitivity test.

2.2.2. Activity testing:

The activities of the samples were determined by agar-well diffusion method. The bacterial isolates were first grown in nutrient broth (Oxoid UK). The zone inhibition of the samples was observed after 24 h incubation at 37°C. The sensitivity effects were compared with kanamycin standard antibiotic at a concentration of 1 mg/ml [15].

3. Results And Discussion

Antimicrobial activities of the test samples are expressed by measuring the zone of inhibition observed around the area.

Table 1: Complex abbreviation for antibacterial activity

Complexes No	Complexes	Symbol
1	[Cu(II) (Gly)2(8-HQ)]	A
2	[Cr(III)(Ala)2(Py)2]	B
3	[Cr(III)(Cyst)2(8-HQ)]	C
4	[Fe (Gly)2(8-HQ)]	D
5	[Co(II) (Gly)2(Q) 2]	F
6	[Co(II) (Gly)2(IQ) 2]	G
7	[Cu(II)(Gly)2(Q)2]	H
8	[Cu(II)(Gly)2(IQ)2]	I
9	[Ni(II) (Gly)2(Q) 2]	J

Where, Gly = Glycine, Cyst= Cysteine, Py = Pyridine, Q = Quinoline, IQ = Isoquinoline, 2-Pico = 2-Picoline, 8-HQ= 8-hydroxyquinoline

The results revealed that the complexes were more toxic to microorganisms than that of the free metal ions or ligands. All the complexes of metals under investigations showed more or less activities against the seven pathogenic bacteria tested.

Table 2: Antibacterial activities of the compound A, B, C, D and Kanamycine (K-30)

Sl. No.	Bacteria	Gram Staining	Diameter of zone inhibition (in mm)				
			A 100 µg/disc	B 100 µg/ disc	C 100 µg/ disc	D 100 µg/disc	K- 30 µg/ disc
1	*Bacillus subtilis*	Positive	6	30	22	8	22
2	*Staphylococcus aureus*	Positive	21	0	0	9	22
3	*Bacillus cereus*	Positive	19	3	2	8	20
4	*Streptococcus agalactiae*	Positive	19	1	0	16	20
5	*Escherichia coli*	Negative	20	0	5	17	25
6	*Shigella dysenteriae*	Negative	19	0	0	19	21
7	*Shigella sonnei*	Negative	15	0	3	0	15

From the zone of inhibition, it is observed that the

complexes A, H, I of Cu(II); B, C of Cr(III); D of Fe(III); and F, G of Co(II), and J of Ni(II) amine bases and amino acid exhibited greater susceptibilities towards all the bacteria used. The results also revealed that among all the tested samples, these metal complexes showed strong activity against both the Gram positive and Gram-negative bacteria (Table-2 and 3).

Table 3: Antibacterial activities of the compound F, G, H, I, J and Kanamycine (K-30).

Sl. No.	Bacteria	Gram Staining	Diameter of zone inhibition (in mm)					
			F 100 µg/ disc	G 100 µg/ disc	H 100 µg/ disc	I 100 µg/ disc	J 100 µg/ disc	K 30 µg/ disc
1	*Bacillus subtilis*	Positive	6	30	22	8	7	22
2	*Staphylococcus aureus*	Positive	8	27	23	9	11	25
3	*Bacillus megatherium*	Positive	6	31	24	7	10	24
4	*Escherichia coli*	Negative	5	29	25	7	5	24
5	*Shigella dysenteriae*	Negative	4	27	26	5	3	21
6	*Shigella sonnei*	Negative	4	27	31	5	7	15

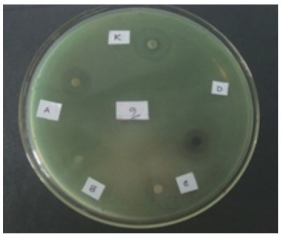

Fig. 1: Photographic representation of zone of inhibition of complexes A, B, C and D, against *Escherichia coli*.

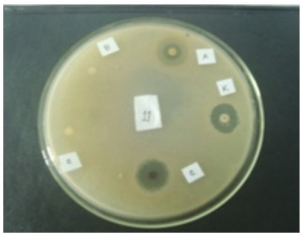

Fig. 2: Photographic representation of zone of inhibition of complexes A, B, C and D against *Shigella dysenteriae*

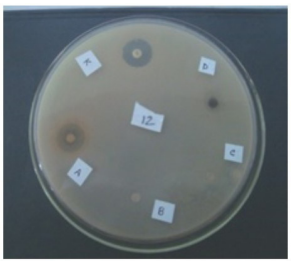

Fig. 3: Photographic representation of zone of inhibition of complexes A, B, C and D against *Shigella sonnei*

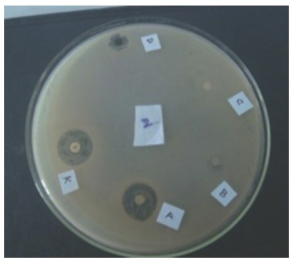

Fig. 4: Photographic representation of zone of inhibition of complexes A, B, C and D against *Staphylococcus aureus*.

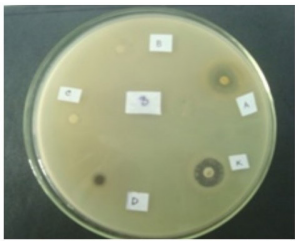

Fig. 5: Photographic representation of zone of inhibition of complexes A, B, C and D against *Bacillus cereus*.

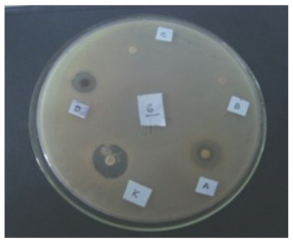

Fig. 6: Photographic representation of zone of inhibition of complexes A, B, C and D against *Bacillus subtilis*.

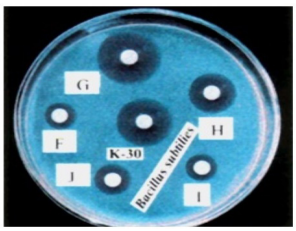

Fig. 7: Photographic representation of zone of inhibition of the complexes F, G, H, I and J against *Bacillus subtilies*.

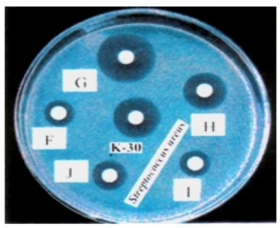

Fig. 8: Photographic representation of zone of inhibition of the complexes F, G, H, I and J against *Staphlococcus aureus*.

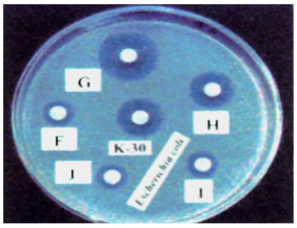

Fig. 9: Photographic representation of zone of inhibition of the complexes F, G, H, I and J against *Escherichia coli*.

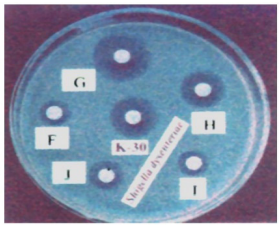

Fig. 10: Photographic representation of zone of inhibition of the complexes F, G, H, I and J *against Shigella dysenteriae*.

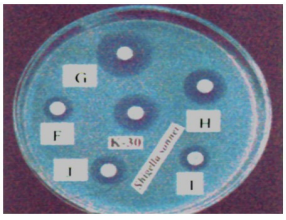

Fig. 11: Photographic representation of zone of inhibition of the complexes F, G, H, I and J against *Shigella sonnei*

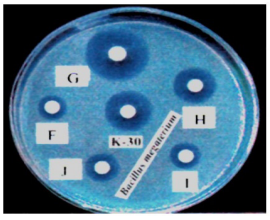

Fig. 12: Photographic representation of zone of inhibition of the complexes F, G, H, I and J against *Bacillus megatherium*

4. Conclusion:

The results showed that the metal complexes have positive scenario on antimicrobial properties. All the microorganisms examined showed high to moderate susceptibility to the tested compounds, good growth and easily visualized colonies, which make them useful for evaluation studies involving antibacterial activity of metal complexes as well as other compounds. The highest inhibition zone was observed for Co (II) complex against *Bacillus megatherium*. But Cr (III) complex showed good antimicrobial property on an average against all mentioned bacteria. In our further work, the antimicrobial activity against all other pathogenic bacteria will be studied and their toxicity level will be measured for therapeutic application.

References:

1. Bauer AW, Kirby WM, Sherris JC, Turck M. Antibiotic susceptibility testing by a standardized single disk method. *American journal of clinical pathology*. 1966;45(4):493.

2. Gnanamanickam SS, Smith DA. Selective toxicity of isoflavonoid phytoalexins to gram-positive bacteria. *Phytopathology*. 1980;70(9): p. 894-896.

3. McLennan A, Bates A, Turner P, White M. Bios instant notes in molecular biology. Taylor & Francis; 2012 Nov 27.

4. Rafique S, Idrees M, Nasim A, Akbar H, Athar A. Transition metal complexes as potential therapeutic agents. *Biotechnology and Molecular Biology Reviews*. 2010;5(2): p. 38-45.

5. Prachayasittikul V, Prachayasittikul S, Ruchirawat S, Prachayasittikul V. 8-Hydroxyquinolines: a review of their metal chelating properties and medicinal applications. *Drug design, development and therapy*. 2013;7: p. 1157-1178.

6. Scheibel LW, Adler A. Antimalarial activity of selected aromatic chelators. II. Substituted quinolines and quinoline-N-oxides. *Molecular Pharmacology*. 1981;20: p. 218-223.

7. Scheibel LW, Adler A. Antimalarial activity of selected aromatic chelators. III. 8-Hydroxyquinolines (oxines) substituted in positions 5 and 7, and oxines annelated in position 5, 6 by an aromatic ring. *Molecular Pharmacology*. 1982;22(1): p. 140-4.

8. Scheibel LW, Adler A. Antimalarial activity of selected aromatic chelators. *Molecular pharmacology*. 1980;18(2): p. 320-5.

9. Sadler PJ. The biological chemistry of gold: a metallo-drug and heavy-atom label with variable valency. *In Biochemistry*, Springer, Berlin, Heidelberg. 1976;29: p. 171-214.

10. Cowan JA. Inorganic biochemistry: an introduction. John Wiley & Sons; 1997 Mar 21.

11. Baulieu E, Forman DT, Ingelman-Sundberg M, Jaenicke L, Kellen JA, Nagai Y, *et al*. Ruthenium and other non-platinum metal complexes in cancer chemotherapy. *Springer Science & Business Media*; 2013 Mar 7.

12. Bertini I, editor. Biological inorganic chemistry: structure and reactivity. University Science Books; 2007.

13. Kudrat-E-Zahan M, Al-Bari MA, Bashar MA, Banu LA, Haque MM, Islam MS. Synthesis, Characterization and Biological Activity of Fe (III) Complexes with tartaric acid/succinic acid and heterocyclic amines. *International Journal of Materials Chemistry and Physics*.2015;1(1): p. 82-5.

14. Banu LA, Kudrat-E-Zahan M, Bashar MA, Haque MM, Quamruzzaman M, Islam MS. Studies on synthesis and characterization with antimicrobial activity of mixed ligand coordinating co (ii) Complexes with phthalic acid and heterocyclic amines. *IJCS*. 2015;2(6): p. 38-41.

15. Irobi ON, Moo-Young M, Daramola SO. Antimicrobial activity of Annato bixoovellana extra. *Int. J. Pharm*. 1996;34: p. 87-90.