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Antimicrobial Studies of Metal Complexes of Fe(III), Co(II) and Ni(II) with Cyanex-272

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Metal cheletes of Fe(III), Co(II) and Ni(II) with bis(2,4,4-trimethyl pentyl)phosphinic acid (cyanex-272; abbreviated as LH) were synthesized. The prepared complexes have the compositions: 1. [Fe(L)3], 2. K[Co(L)3] and 3. [Ni(L)2]. Their conventional physical and chemical analysis had been done. Their anti-bacterial and antifungal activity had been evaluated. Disc diffusion methods were employed for antimicrobial assays against four human pathogenic bacteria and fungi. The biological properties of the metal complexes reveal that the complex 3 is more effective against almost all antibacteria tested. Furthermore, the complexes 1 and 3 show the height antifungal activity against the fungi *Trichophyton sp*. and *Aspergillus flavus*.

Keywords: Antibacterial activity, antifungal activity, cyanex-272.

The frequency of life threatening infections such as tuberculosis, cancer, AIDS etc caused by pathogenic microorganisms is increasing worldwide and becoming an important cause of morbidity and mortality in immunocompromised patients. Synthetic chemical compounds constitute important sources of various bioactive compounds such as antibacterial,[1] antifungal[2] and anticancer[3] compounds. The synthesized chemical compounds, which are used for the treatment of infectious diseases, are known as chemotherapeutic agents. Every year thousands of compounds are synthesized with an aim to find a potential chemotherapeutic agent to combat pathogenic microorganisms. Fe(III), Ni(II), Co(II) and Cu(II) complexes with thiazoline and their fungicidal activity has been evaluated[4]. Metal chelation or complexation is involved in many important biological process, where the co-ordination can occur between a variety of metal ions and a wide range of ligand.[5] Many types of ligand are known and the properties of their derived metal chelate have been investigated[6]. Prior to 1980, search for anticancer drugs was focused primarily on organic compounds.[7] However, with the discovery of cis-diammine dichloro platinum (II), which shows excellent antitumour activity, keen interest arose in exploring other inorganic compounds as possible therapeutic agents. Copper, silver and gold complexes are among the most promising inorganic compounds known to possess anticancer activity.[7] Copper is found in human cells and is primarily associated with copper-dependent enzymes that are required for normal metabolic

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process. The complexation of CO, Fe, Mg, Zn and Cu with nitrogen containing chain in the enzymes are very diverse.[8] The antimalarial activities of a series of 2-acetyl pyridine and their Cu, Ni, Fe, and Mn complexes have been tested for their antimalarial and antileukemic properties.

These compounds have been found to possess significant antimalarial activities[9]. Virtually it is clear that some compounds, which have therapeutic actions, have increased reactivity when these are complexed with metal ions. There are many metallic compounds which have pharmacological effect and used as active ingredients.[10] Pharmaceutically so far the most important complexes are ferrous fumarate and ferrous gluconate (hematinies), gallium citrate (diagnostic agent), Magnesium salicylate (antirheumatic arthritic agent), sodium cromoglycate (anti-asthma), etc.[11]

The aim of this study was to determine the antimicrobial activity of compounds of some transition metal Fe(III), Co(II) and Ni(II) with Cyanex-272 as bidentate ligand for development as potential new antibiotic or chemotherapeutic agent *in vitro* antimicrobial screening is useful technique. In general, antimicrobial screening is under taken in a primary qualitative assay to detect the presence or absence of activity of a pure active compound.

MATERIAL AND METHODS

The coordination complexes were obtained from the Inorganic Chemistry Research Laboratory of Rajshahi University, Bangladesh, where these were prepared and characterized[12]. The tested bacteria and fungi were collected from the Department of Botany, University of Rajshahi. All steps of the work were carried out at the Plant-Pathology and mycology laboratory, Department of Botany, University of Rajshahi Bangladesh.

Preparation of complexes

Metal chlorides were used in preparation of metal ion solutions. The metal chelates were prepared by agitating 0.015 mol dm^{-3} of K-salt of Cyanex-272 in absolute alcohol with Fe(III), Co(II) and Ni(II) separately in their 0.005 mol dm^{-3} ethanolic salt solutions. These mixtures were stirred, wamed in water bath and allowed to stand at room temperature. The crystalline precipitates found were collected by filtration, washed several times with ethanol, then with distilled water (to remove KCl formed) and finally dried in vacuum desiccators over P_4O_{10} for a fortnight. Preparation of K-salt of Cyanex-272 was made by mixing together 4.35 g dm^{-3} and 0.56 g dm^{-3} respectively of Cyanex-272 and KOH in absolute alcohol. The mixture was stirred well and heated on a water bath for 2-3 hours to reduce it to 50cm^3, it was then allowed to stand at room temperature for several hours. The precipitate of K-salt of Cyanex-272 formed was reprecipitated, collected by filtration, washed with ethanol and finally dried in vacuo over P_4O_{10}.

Antibacterial assay

In vitro antibacterial screening is generally performed by the disc diffusion method[13] for primary selection of the compounds as therapeutic agents. The method is highly effective for rapidly growing microorganisms and the activities of the test compounds are expressed by measuring the diameter of the zone of inhibition. Generally, the more susceptible the test organism, the larger is the zone of inhibition. The method is essentially a qualitative or semi quantitative test indicating sensitivity or resistance of microorganisms to the test materials as well as the bacteriostatic or bactericidal activity of a compound[14]. The complexes were screened for antibacterial activity against *Streptococcus-b-haemolyticus* (Gram positive), *Bacillus subtilis* (Gram positive), *Salmonella typhi* (Gram negative) and *Escherichia coli* (Gram negative). The activities were carried out with the help of disc diffusion technique.[15,16] Each disc contained 100 mg of compound and it was placed on bacteria inoculated plates. The growth inhibition results were compared with standard antibiotic Kanamycin(K-30) and either carbon tetrachloride (CCl_4) or dimethylsulfoxide (DMSO), which were used as control.

Antifungal assay

The antifungal activity of the complexes carried out against *Tricophyton* sp., *Penicillium* sp., *Aspergillus flavus a*nd *Bipolaris sorokiniana,* by the activities were carried out with the help of disc diffusion technique[15,16] . The compounds were dissolved in eirher carbon tetrachloride (CCl_4) or dimethylsulfoxide (DMSO) and each disc contained 100 mg compound. Antifungal activity

Table 1. Results of the antibacterial activity of the complexes (1-3)

Name of the bacteria	Bacterial zone of inhibition (mm) bacteria in different complexes			
	1	2	3	Kanamycin
	100 µg/disc	100 µg/disc	100 µg/disc	30µg/disc
Streptococcus-b-haemolyticus (+ve)	7	10	16	15
Bacillus subtilis (+ve)	6	10	15	17
Salmonella typhi (-ve)	9	12	15	16
Escherichia coli (-ve)	5	10	18	15

Table 2. Results of the antibacterial activity of the complexes (1-3)

Name of the fungi	Fungal zone of inhibition (mm) in different complexes			
	1	2	3	Fluconazol
	100 µg/disc	100 µg/disc	100 µg/disc	30µg/disc
Trichophyton sp.	15	11	14	10
Penicillium sp.	0	5	0	16
Aspergillus flavus	*12*	*10*	*16*	*14*
Bipolaris sorokiniana	0	0	0	18

of the compound was compared with standard antifungal agent Fluconazol(F-30) and either CCl_4 or DMSO, which were used as control.

RESULTS AND DISCUSSION

Antibacterial activity

The antimicrobial activity of the compounds 1,2 and 3 were determined at the concentration of 100 mg/disc against a series of Gram positive and Gram negative pathogenic organisms. The complex 3 showed more activity against the tested bacteria than others. The compound 2 also has shown substantial antimicrobial activity. The zones of inhibition were found as 18 mm for the complex 3 against *Escherichia coli* (-ve) (Table 1). It may concluded that most of the complexes have antibacterial effect except complex no. 1, which has less antibacterial effect.

Antifungal activity

Table 2 showed that the complexes 1 and 3 were the highest antifungal activity against the fungi *Trichophyton* sp. and *aspergillus flavus*. All the complexes have not shown antifungal activities against the fungi *Bipolaris sorokiniana*. But the lowest antifungal activity against the fungi *Penicillium* sp. (5 mm). The zone of inhibition against *Aspergillus flavus* and *Trichophyton* sp. was found to be 16 and 14 mm for complex 3. Complex 3 and complex 1 showed maximum activity against the tested *Aspergillus flavus* and *Trichophyton* sp.

CONCLUSION

The Nickel complex showed biocidal activity against bacteria and fungi. Further studies of the nickel complex may explore its clinical implications in the world most life threaten disease cancer.

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