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Studies on Biological Activities of Some Chiral Cobalt Complexes

KEYWORDS

Sunny S. Tarve	Sagar V. Sanap	Raju M. Patil
Department of Chemistry, The Institute of Science, 15 Madam Cama Road, Mumbai, India.	Department of Chemistry, The Institute of Science, 15 Madam Cama Road, Mumbai, India.	Department of Chemistry, The Institute of Science, 15 Madam Cama Road, Mumbai, India.

ABSTRACT A series of ternary Cobalt(II) Chiral mixed ligand (CML) complexes of the type [Co(MINAP)(aa)·2H2O] were prepared with sodium salt of p-methylisonitrosoacetophenone as primary ligand, CoSO4.7H2O and chiral amino acid (aa) like L-alanine, L-valine, L-leucine, L-methionine and L-phenylalanine as secondary ligand. The chiral complexes were characterized by elemental analysis and various physicochemical techniques. The antibacterial and antifungal activity of the CML complexes were studied by paper disc diffusion method and Tube dilution method respectively against some pathogenic bacteria like E. coli, S. typhi and S. aureus and some pathogenic fungi C. albicans and A. niger.

INTRODUCTION

The synthesis and study of coordination compounds containing biologically important ligands have been paid much attention in recent years because of their wide applicability in biological, environmental and other system[1]. The vast majority of compounds are used for substitution of essential metal ions and for maintaining their appropriate concentration[2]. Many of the inorganic medicinal compounds are mixed ligand complexes[3]. Cobalt is present in vitamin B_{12}, a co-enzyme that plays significant roles in some biochemical processes[4]. A new chiral amino acid Schiff base ligand (Salarg) and its metal complex (Mn-Salarg) have been synthesized using L-Arginine, a naturally occurring chiral diamine with two kinds of asymmetric α-, ε-,-NH_2 groups by Roy[5]. Some gold complexes have been used as injections to reduce the pain and swelling of rheumatoid arthritis and tuberculosis[6]. Amino acids are well known of their biological importance as structure units that build up proteins, and their common use in nutritional supplements, fertilizers and food technology[7-9].

Experimental

Materials: The A.R. grade chemicals were used as such without further purification. The sodium salt of p-methylisonitrosoacetophenone was prepared[10] by using the reported method. L-alanine, L-valine, L-leucine, L-methionine and L-phenylalanine are the various chiral amino acids used as secondary ligand which brought from THOMAS BAKER. All the solvents to be used were distilled and purified according to standard procedures[11].

Methods:

(1)Preparation of Complexes: The aqueous solutions (1mmol) each of Co(II) sulphate heptahydrate and sodium salt of p-methylisonitrosoacetophenone mixed with constant stirring and then kept in a boiling water bath for 30 minutes. The mixture was cooled. An equimolar (1mmol) aqueous solution of the sodium salt of chiral amino acid was added to it and heated for three hours in a hot water bath. Solid complexes were filtered off, washed first with ice-cold water followed by 1:1 ethanol:water. Complexes were dried under vacuum.

Synthesis of present complexes may be represented by following equation

$$Co(II) + Na\text{-}MINAP + Na\text{-}aa \rightarrow (-)[Co(MINAP)(aa)] + 2Na^{+}$$

Where Na-MINAP: Na salt of p-methylisonitrosoacetophenone, Na-aa: Na salt of L-amino acid.

The complexes thus formed were characterised by elemental analysis and various physicochemical techniques[12].

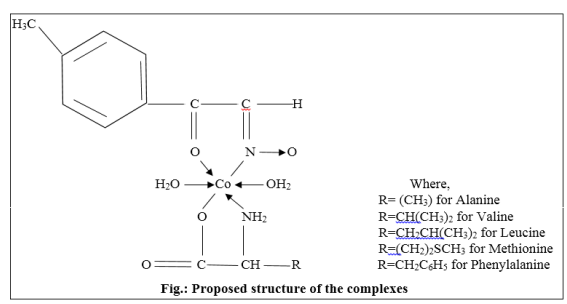

Fig.: Proposed structure of the complexes

(2)Biological Studies:

Broth Dilution Method: Using this method the Minimum Inhibition Concentration (MIC) of complexes was found[13-14]. The nutrient media used for antibacterial activity was Muller Hinton Broth and Sabouraud Broth used for antifungal activity. Firstly the 1000ppm concentration individual stock solution of each complex in DMSO was prepared. Further required dilutions were made by using respective Broth medium. The 200ppm, 300ppm and 400ppm concentrations of the complexes taken for each microbial species.

Paper Disc Diffusion Method: The antibacterial activity of the complexes against *E.coli*, *S.typhi* and *S.aureus* pathogenic bacteria was tested using Paper Disc Diffusion Method. The 0.1mL inoculums of the test organism was spread uniformly on the surface of the agar medium in a petri plate by using a spreader. The 5 mm diameter sterilized Whatmann filter paper discs were sterilized, dipped into the 400ppm solution of the complexes in DMSO and were placed on the surface of the agar in each plate. The plates were placed in incubator at 37°C for 24 hours. The complex diffuses from the filter paper into agar during incuba-

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tion. The diameter of the inhibited zone was measured in millimeters (mm). This will be used to assess the activity of the complexes. The results of all the complexes were compared against that of the control (tetracycline) which was screened simultaneously. Solvent DMSO, used as blank, was also run to know its activity.

Tube Dilution Method: Using this method antifungal activity of the complexes was obtained against *C.albicans* and *A.niger* pathogenic fungi. For the preparation of fungus inoculums the selected fungus was inoculated into sterilized Sabouraud broth. 0.1 mg per mL of streptomycin was added to prevent bacterial contamination. After sporulation the spores were harvested in the same media by gentle stirring using a magnetic stirrer and the spore suspension was poured into another sterile flask. 5mL of Sabouraud broth was taken in a 15 mL Corning test tube and 0.1mL of 300ppm solution of the complexes in DMSO was added to it. It was autoclaved at 15 lb pressure for 15 minutes. The tubes were then kept on a rotary shaker and incubated at room temperature for 24 hours. The optical density (OD) of the solution was determined using a spectrophotometer at 530 nm with inoculated Sabouraud broth as blank and on the basis of optical density the percentage growth of the fungus was calculated. The growth of the fungus in the tube without an antifungal agent was assumed as 100%. The results were compared against those of the control (amphotericin), which was screened simultaneously.

Results and Discussions:

The antimicrobial activity of all the complexes is less than that of standard tetracycline and amphotericine. Secondary ligand amino acids did not show antibacterial and antifungal activity. The activity of metal sulphate and primary ligand is significantly enhanced on complexation. The MIC of present CML complexes at which the culture does not show bacterial and fungal growth were found to be 400ppm and 300ppm respectively. The antibacterial and antifungal activity data is shown in table.

Table : Biological activity of the CML Co(II) complexes

Complex	Antibacterial activity at 400ppm (zone of inhibition in mm)			Antifungal activity at 300ppm (% Inhibition)	
	E.coli	S.typhi	S.aureus	C. albicans	A. niger
[Co(MINAP)(Ala).2H_2O]	6	6	7	42	50
[Co(MINAP)(Val).2H_2O]	5	4	7	37	54
[Co(MINAP)(Leu).2H_2O]	6	6	7	47	58
[Co(MINAP)(Met).2H_2O]	7	8	8	52	61
[Co(MINAP)(Phe).2H_2O]	3	3	4	40	52
Na-MINAP	3	2	3	16	14
$CoSO_4$.7H_2O	3	2	4	34	32
Tetracycline	14	15	13	-	-
Amphotericin	-	-	-	97	98

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