Research Paper Chemistry

Studies on Biological Activities of Some Chiral Nickel Complexes

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ABSTRACT

Some new Chiral mixed ligand (CML) ternary Nickel complexes [Ni(MINAP)(aa)·2H2O] have been prepared with reaction of Ni(II) metal, sodium salt of p-methylisonitrosoacetophenone as primary ligand and chiral amino acid (aa) as secondary ligand such as L-alanine, L-valine, L-leucine, L-methionine and L-phenylalanine by 1:1:1in situ stereoselective complexing. The CML complexes thus formed were characterized by the virtue of elemental analysis, molar conductance, specific optical rotation, room temperature magnetic susceptibility, electronic absorption, infrared spectral and TG-DTA analysis. The antibacterial activity of the CML complexes checked by paper disc diffusion method against some pathogenic bacteria like E. coli, S. typhi and S. aureus. Tube dilution method was used to study antifungal activity of complexes against C. albicans and A. niger pathogenic fungi. The results have been compared with those of tetracycline for antibacterial and amphotericin for antifungal activity, which were screened simultaneously.

KEYWORDS

INTRODUCTION

Transition metal ions are known to play very important roles in biological processes in the human body. For example, Zn(II) and Cu(II) ions are the second and third most abundant transition metals in humans. Many researchers have studied characterization, antimicrobial and toxicological activity of mixed ligand complexes of transition metals[1-4]. Mixed ligand complexes are generally found to be more active biologically than the ligand itself[5]. A list of metal containing compounds used in chemotherapy for treatment of diseases include platinum (anticancer), silver (antimicrobial), gold (antiarthritic), bismuth (antiulcer), antimony (antiprotozoal), vanadium (antidiabetic) and iron (antimalaria)[6]. The biological importance of some potential chiral compound like hydroxyazole bioisosteres of glutamic acid and some Novel bicyclic acidic amino acids is well known[7-9].

Experimental

Materials: All the chemicals used were having Analytical Grade purity. The sodium salt of p-methylisonitrosoacetophenone was prepared[10] by using the reported method. Various chiral amino acids such as L-alanine, L-valine, L-leucine, L-methionine and L-phenylalanine obtained from THOMAS BAKER and were used directly without further purification. All the solvents to be used were distilled and purified according to standard procedures[11].

Methods: (a)Preparation of Complexes:

To the aqueous solution (1 mmol) of Ni(II) sulphate heptahydrate and an aqueous solution (1mmol) of sodium salt of p-methylisonitrosoacetophenone was added slowly with constant stirring on magnetic stirrer. This mixture then kept in a boiling water bath for 30 minutes. Cooled and added an aqueous solution (1mmol) of the sodium salt of chiral amino acid and final mixture was heated for three hours in a hot water bath. Solid complexes were obtained by filteration, washed first with ice-cold water followed 1:1 ethanol:water. Complexes were dried under vacuum. Synthesis of present complexes may be given by following equation.

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

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

The CML complexes were characterised by elemental analysis and different physicochemical techniques[12].

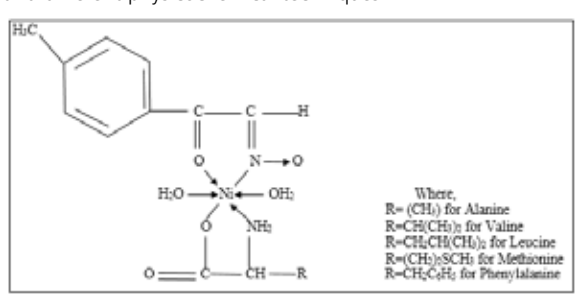

Fig: Proposed structure of the complexes

(b) Biological Studies:

Broth Dilution Method: The Minimum Inhibition Concentration (MIC) of complexes was found by Broth Dilution Method[13] using Muller Hinton Broth for antibacterial activity and Sabouraud Broth for antifungal activity as the nutrient media. The individual stock solution of 1000ppm concentration of each complex in DMSO was prepared first and then further dilutions were prepared as per requirements using respective Broth medium. The concentrations of the complexes taken for each microbial species were 200ppm, 300ppm and 400ppm.

Paper Disc Diffusion Method: The antibacterial activity of the complexes was studied using this method against *E.coli, S.typhi* and *S.aureus* pathogenic bacteria. The 0.1 mL of inoculums of the test organism was spread uniformly on the surface of the agar medium in a petri plate by using a spreader. The Whatmann filter paper discs of 5 mm diameter were ster-

ilized and dipped into the 400ppm solution of the complexes in DMSO. Up to four discs were placed on the surface of the agar in each plate. The plates were incubated at 37°C for 24 hours. During incubation, the complex diffuses from the filter paper into agar. The activity of the complexes was assessed by measuring the diameter of the inhibited zone in millimeters (mm). The control (tetracycline) was screened simultaneously along with the CML complexes and the results of all the complexes were compared against it. Solvent DMSO, used as blank, was also run to know its activity.

Tube Dilution Method: The antifungal activity of the complexes against *C.albicans* and *A.niger* pathogenic fungi was determined by this method. The selected fungus was inoculated into sterilized Sabouraud broth to form fungus inoculums. The bacterial contamination was prevented by adding 0.1 mg per mL of streptomycin to fungus inoculums. 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. Then 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 control (Amphotericin) was screened simultaneously and the results were compared against it. The growth of the fungus was assumed as 100% in the tube without an antifungal agent.

Results and Discussions:

Most metal complexes show biological activity in chelate form[14-15]. It has been observed that the complexes inhibit protein synthesis and act by binding to the ribosome[16]. The binding, however, is not tight and when the concentration of the complex becomes free from the ribosome the growth is resumed. 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. Amino acids used for current investigation did not show antibacterial and antifungal activity while the antimicrobial activity of metal sulphate and primary ligand is significantly enhanced on complexation. Compared to standard antibacterial and antifungal compounds tetracycline and amphotericin, the present CML complexes are less active. The antibacterial and antifungal activity data of CML complexes, sodium salt of p-methylisonitrosoacetophenone, nickel sulphate, tetracycline and amphotericin is shown in table.

Table: Biological activity of the CML Ni(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
[Ni(MINAP)(Ala)·2H2O]	5	6	6	40	54
[Ni(MINAP)(Val)·2H2O]	5	4	6	39	52
[Ni(MINAP)(Leu)·2H2O]	7	8	8	44	57
[Ni(MINAP)(Met)·2H2O]	7	6	8	48	58
[Ni(MINAP)(Phe)·2H2O]	4	5	5	39	51
Na-MINAP	3	2	3	15	14
$NiSO_4.7H_2O$	3	2	4	32	30
Tetracycline	14	15	13	-	-
Amphotericin	-	-	-	97	98

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