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Studies on Mixed Ligand Complexation of Aluminium by Some Natural Amino Acids and hydroxy Acids.

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ABSTRACT

Mixed ligand aluminium complexes involving some natural amino acids viz., glycine, α-alanine, L-aspartic acid or L-glutamic acid and some natural hydroxy acids viz., malic, tartaric or citric acid have been synthesized in aqueous medium at room temperature. Analytical results suggest the complexes to be of formulae, [Al(gly)(mal)], [Al(gly)(tart)], [Al(gly)(H.cit)], [Al(aln)(mal)], [Al(aln)(tart)], [Al(aln)(H.cit)], [Al2(asp)2(mal)], [Al2(asp)2(tart)], [Al2(asp)2(H.cit)], [Al2(glu)2(mal)], [Al2(glu)2(tart)] and [Al2(glu)2(H.cit)], where, gly, aln, asp, glu, mal, tart and H.cit are glycinate, α-alaninate, L-aspartate , L-glutamate, malate , tartrate and citrate (dibasic) respectively. In the infrared structure, the stretching and bending modes of NH2 group of amino acids have been found to split into two or shift from their position upon complexation. This suggest a coordinated nature of amino group in the complexes. Evidence for additional hydrogen-bonding in the complexes, involving, possibly, the OH groups of hydroxy acids and NH2 groups of amino acids , is also observed in the infrared spectra of complexes. The 1H NMR spectra of the ligands and complexes also suggest coordination of NH2 group of amino acids in the complexes. Utility of the results in aluminium toxicology has been discussed.

Keywords: Aluminium complexes, Amino acid complexes, Mixed ligand complexes, Aluminium toxicity, Aluminium biotoxicology.

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INTRODUCTION

Aluminium is the most abundant metal in the earth's crust. Despite abundance, aluminium does not have any useful biological function. Rather, it causes potential toxicity and health hazard when ingested in excess.1 Aluminium ingestion has been implicated in diseases like osteomalacia2, dialysis encephalapathy3,4 and Alzheimer's disease5,6. Aluminium may enter into the body through food, water or air borne dust particles. Alfrey et al.7,8 have proved the detrimental effect of aluminium neurotoxicity. In Alzheimer disease abnormal accumulation of aluminium in the brain has been shown9,10. It has also been recently hypothesized that aluminium could be involved in binding to the hyperphosphorylated tau proteins in this disease.11 Studies in aluminium biotoxicology has recently been receiving much attention12-25. The neurotoxicity of aluminium might involve its complexation with bio-compounds. The involved complexation equilibria might be either of pure ligand or of mixed ligand type. Mixed ligand equilibria are infact found in most solutions in natural systems. As such, an investigation into the coordination chemistry of aluminium in the vicinity of natural compounds, particularly in the mixed ligand environment, would reveal more about the mechanism of its biotoxicity. Such studies would also be helpful in designing drugs for aluminium detoxification. With the above views in mind, we have presently studied the mixed ligand complexation of aluminium involving some natural amino acids viz., glycine, α-alanine, L- aspartic acid or L-glutamic acid and some natural hydroxy acids viz., malic, tartaric or citric acid.

MATERIALS AND METHODS

All chemicals used were of A.R. (Analytical Reagent) quality. Preparation of Complexes:- 0.015 mole of amino acid (glycine, α-alanine, L-aspartic acid or L-glutamic acid) was suspended in 25 ml of distilled water. Dilute NaOH solution was added drop wise, with constant stirring to neutralize the solution (pH-7). The amino acid got dissolved and a clear solution was obtained. Next, 0.015 mole of hydroxy acid (malic acid, tartaric acid or citric acid) was added to the solution. The hydroxy acid got dissolved and a clear solution was obtained. Next, 0.005 mole of aluminium acetate was added to the solution. The reaction mixture was stirred for 4h, on a magnetic stirrer at room temperature. The pH was maintained at 7 during the reaction. At the end, the reaction mixtures were clear. The complexes were separated from the reaction mixture by crystallization. The crystals were filtered, washed with small quantity of distilled water and dried at 110◦ C in an air oven and preserved over anhydrous calcium chloride.

Analysis of Complexes

A known weight of complex was decomposed by 10 ml of conc. HNO3 by heating and evaporating to dryness. The dry residue was extracted with distilled water to a known volume (100 ml) into a measuring flask. Aluminium in the solution was estimated spectrophotometrically using Eriochrome Cyanine R reagent26 . C, H & N were estimated microanalytically.

Infrared Spectra

FTIR spectra of ligands and complexes have been recorded in KBr phase in the range of 4000-450 cm-1, on a Excalibur HE3600 infrared spectrophotometer.

NMR Spectra

1H NMR spectra of ligands and complexes were recorded in DMSO- d6, on a Bruker Avance II 400 NMR Spectrometer.

RESULTS AND DISCUSSION

Compounds were found to be stable when stored under dry condition. Analytical data of the compounds are recorded in Table-1. Analytical results suggest a metal : amino acid ligand : hydroxy acid ligand mole ratio of 1 : 1 : 1 in case of amino acid viz., glycine or α-alanine and hydroxy acid viz., malic, tartaric or citric acid complexes; and 2 : 2 : 1 in case of amino acid viz., L-aspartic or L-glutamic acid and hydroxy acid viz., malic, tartaric or citric acid complexes.

Infrared Studies

FTIR spectra of ligand and complexes have been recorded in KBr phase in the range of 4000 – 450 cm-1. The mixed ligand complexes of aluminium involving amino acid (glycine, α-alanine, L-aspartic acid or L-glutamic acid) and hydroxy acid (malic, tartaric or citric acid) mostly show two strong bands in the region around 3400 and 3000 cm-1. These band might be assigned to the doubly split NH stretching vibration. The first band at 3400 has mostly been found to be rather broad. The υOH of hydroxy acids might also be showing at this region. Thus, the υNH and υOH showing at about same place. The position of υOH (of hydroxy acid) at rather low (below 3600) might be due to involvement of OH of hydroxy acids, either in coordination to the metal or its involvement in H-bonding with a suitable neighbouring groups within the molecules. Additional band (low intensity and sharp) is invariably shown at approximately 2400 in the spectra of all the complexes. This further substantiate a state of H-bonding in the complex. The split of υNH in the complexes, as compared to a single band in the pure amino acid spectra (for υNH) suggest coordination of NH2 of amino acid moity to the metal in the complex. The bending mode of NH is mostly traced at 1626 cm-1 in the case of all the complexes.

Thus, it seems the amino acid and hydroxy acid form the mixed ligand complex with aluminium by deprotonation of COOH groups as well as additional coordination through NH2 groups of amino acids and OH groups of hydroxy acids. Since the complexation with aluminium would be rather weak (Al is a non transition metal), it is difficult to pin-point between coordinated and H-bonded NH2/OH groups. In any case, the IR spectra of mixed complexes strongly suggest the involvement of donor groups of the ligands, in bonding to the metal within the complex. The amino acid and hydroxy acid that we have studied with contain a number of functional groups showing sharply in the finger print region. As such, the exact pin-pointing of the mode of bending in these complexes through IR spectra would be rather difficult.

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NMR Studies

In the 1H NMR of mixed ligand aluminium complexes involving amino acids and hydroxy polybasic acids, the CH protons show strong signal at δ 3.3 – 3.4. A medium intensity signal occurring at δ 8.0 – 8.1 can be assigned to the OH proton of alcoholic or carboxylic group. Since the ligand in the complex have a number of OH and COOH groups, pin-pointing of the exact OH proton corresponding to this signal would rather be difficult. It only indicates that definitely there are OH proton in the moity. The NH2 protons of the complex are found as two signals stationed at δ 2.5 and 1.7. Rather down field position of NH signal suggest involvement of NH2 groups in coordination to the metal. The split of NH2 proton signal into two, as compared to a single signal in the case of pure amino acids, suggest further the coordinated nature of amino group of amino acid moity in the complex. Some of the NH2 protons are involved in H-bonding with some suitable neighbouring group in the molecule. Such an involvement would be stabilize the complex. On the basis of analytical and spectral studies, the structure and bonding of the complexes may tentatively be proposed as shown in Fig.1and Fig.2 respectively.

Table-1 Analytical data of compounds

Compounds	Analysis of % found (calculated)			
	Al	C	H	N
[Al(gly)(mal)]	11.23 (11.58)	30.28 (30.90)	3.24 (3.43)	5.82 (6.0)
[Al(gly)(tart)]	10.80 (10.84)	28.36 (28.91)	3.45 (3.21)	5.17 (5.62)
[Al(gly)(H.cit)]	9.60 (9.27)	32.37 (32.98)	3.62 (3.43)	4.37 (4.81)
[Al(aln)(mal)]	10.45 (10.93)	34.12 (34.0)	4.52 (4.04)	5.24 (5.66)
[Al(aln)(tart)]	10.13 (10.26)	31.73 (31.93)	3.53 (3.80)	5.08 (5.52)
[Al(aln)(H.cit)]	8.27 (8.85)	34.91 (35.40)	3.18 (3.93)	4.24 (4.59)
[Al2(asp)2(mal)]	11.62 (12.05)	32.43 (32.14)	3.24 (3.12)	6.08 (6.25)
[Al2(asp)2(tart)]	11.24 (11.63)	30.86 (31.03)	2.84 (3.01)	6.24 (6.03)
[Al2(asp)2(H.cit)]	10.27 (10.67)	33.41 (33.20)	3.46 (3.16)	5.38 (5.53)
[Al2(glu)2(mal)]	10.86 (11.34)	34.67 (35.29)	3.82 (3.78)	5.63 (5.88)
[Al2(glu)2(tart)]	10.43 (10.97)	34.42 (34.14)	3.24 (3.65)	5.17 (5.69)
[Al2(glu)2(H.cit)]	10.32 (10.11)	35.53 (35.95)	3.08 (3.47)	5.12 (5.24)

Where, gly, aln, asp, glu, mal, tart and H.cit are glycinate, α-alaninate, L-aspartate , L-glutamate, malate , tartrate and citrate (dibasic) respectively.

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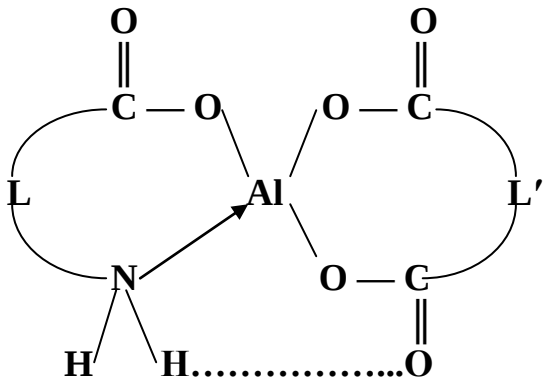

Fig. 1 L = gly or aln
L′ = mal, tart or H.cit

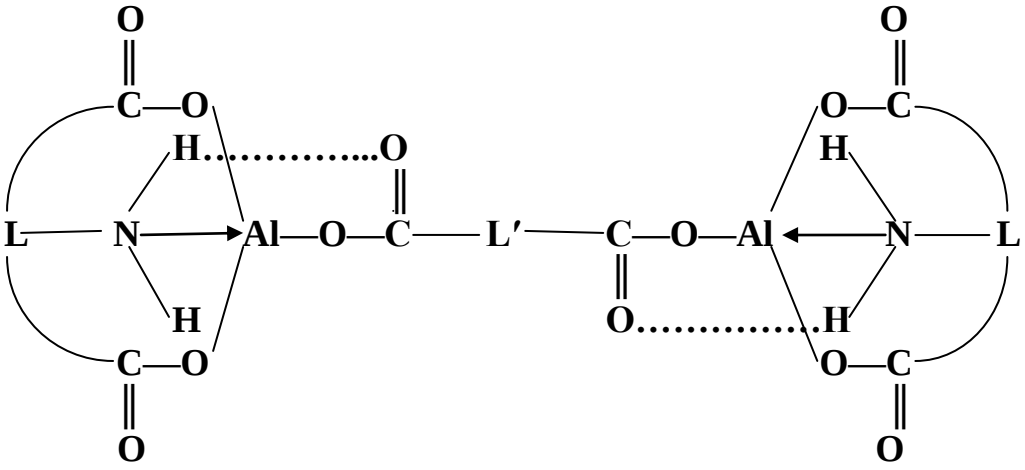

Fig. 2 L = asp or glu
L′ = mal, tart or H.cit

CONCLUSION

The amino acids and the hydroxy acids that we have presently worked with are biologically important ones. The brain has a good amino acid pool and the amino acid (particularly glutamate) serves in many detoxification reactions. The basis of neurotoxicity of aluminium has been suggested to be due to its accumulation in the brain. Role of complexation of aluminium (by hyperphosphorylated tau proteins) in its expression of toxicity has also been hypothesized11. Complexation of aluminium by the amino acids might offer a good protection from Al-toxicity. The complex equilibria might even be of mixed ligand type involving both, amino acids as well as hydroxy acids. This is because the circulating hydroxy acid pool (particularly citrate) is also good, and being oxygen donors, they have a good effinity for aluminium. As such, these amino acids and hydroxy acids could be explored for aluminium detoxification. However, a possibility also exists that complexation of aluminium by the brain amino acids (in case of Al-toxicity) may lead to depletion of brain amino acid pool, leading to adverse affects. As such, aluminium complexation by the natural amino acids and hydroxy acids should be probed in-vivo, in

animal experiments, for a better understanding of the role of complexation in aluminium toxicology.

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