

## STUDY OF THE INTERACTION OF THE NEUROTOXIN Al(III) WITH QUINIC ACID

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### Abstract

*The importance of aqueous aluminum chemistry in biology relates to Al(III) involvement in many neurological disorders such as Alzheimer's disease (AD). The biotoxic role of this metal in neurodegeneration is widely researched nowadays with as yet ambiguous results. In the present study, a new aqueous Al(III)-quinic complex was synthesized. The new species was characterized by elemental analysis, spectroscopic, and structural by X-ray analysis. Detailed aqueous speciation studies in the Al(III)-quinic system suggest the presence of a number of species, among which is the mononuclear  $[Al(C_7H_{11}O_6)_3]^0$  complex.*

**Keywords:** aluminum, toxicity, quinic acid

### Introduction

The presence of quinic acid in nature has been well established. It is present in the plant kingdom, where it constitutes a significant intermediate precursor in the synthesis of shikimic acid, which in turn is involved in the biosynthesis of various essential amino acids and specifically the aromatic ones (Stryer, 1997). Quinic acid has two important structural features: a) it is an  $\alpha$ -hydroxycarboxylic acid. In that respect, it is similar to carboxylic acids present in quantities higher than that in a real biological system and b) it belongs to a category of cyclic polyols, which function as calcium carriers in biological systems.

A natural consequence of such an active participation in biosystems is the tremendous impetus in studying the aqueous chemistry with biotoxic metal ions such as aluminum. That drive rides primarily on the chemical attributes of quinic acid of which most prominent appear to be the large number of functional groups that

contain oxygen. The latter, known hard bases, constitute a natural target for the coordination of hard acids, such as the metal ion Al(III).

The rising interest, on the other hand, in the aqueous chemistry of Al(III) shown in the last decade or so is reflected in the continuing epidemiological studies, showing active involvement of Al(III) in neurotoxic effects and neurodegenerative processes, in which it participates. The latter have been known to lead to biological dysfunctions and ultimately aberrant pathologies with detrimental health results. Among the commonly encountered paradigms of such pathophysiological conditions linked to Al(III) are the following neurodegenerative diseases: Alzheimer's disease (AD) (Crapper, 1976), osteomalacia (Kovalchik, 1978), microcytic anemia (Gitelman, 1989), and others.

The biotoxic role of aluminum in the case of Alzheimer's disease has been under close scrutiny, however, without any tangible evidence for a definitive cause and effect relationship between the two. It has been shown, nevertheless, that amyloid plaques and neurofibrillary tangles in Alzheimer's patients in the terminal stages of the disease are associated with high levels of Al(III) (McLachan, 1986; Perl, 1985).

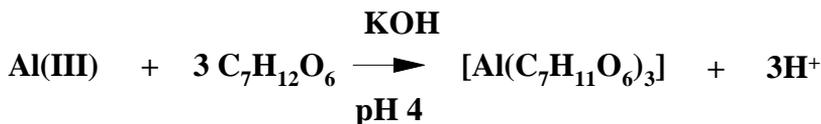
It is, therefore, very important that the aqueous structural speciation of Al(III) involved in binary and ternary systems with physiological substrates-ligands be studied, in an effort to comprehend:

- a) the nature and distribution of soluble species arising from requisite interactions;
- b) the bioavailability of soluble species to which potential biotoxic effects can be ascribed.

One such system under investigation in our labs is the binary Al(III)-quinic acid system.

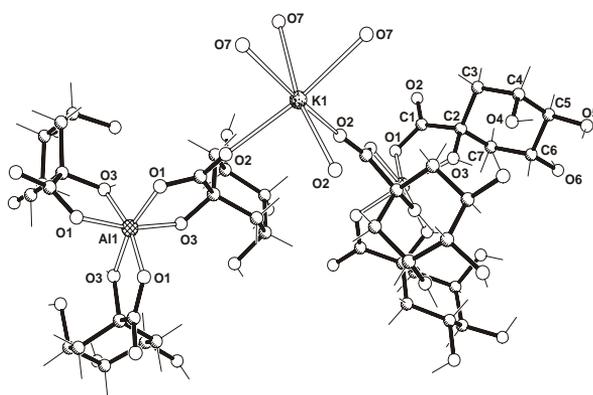
## **Experimental**

The synthesis of the complex  $K[Al(C_7H_{11}O_6)_3](OH) \cdot 5H_2O$  (**1**) was achieved in nanopure water at pH 4. The isolated crystalline product was characterized by elemental analysis, FT-IR spectroscopy, NMR and X-ray crystallography. The reaction leading to the formation and isolation of the title species is given concisely below:



## Results and Discussions

FT-IR spectroscopy was essential in pointing out the coordination of quinic acid to the metal ion Al(III). Equally informative was X-ray crystallography. The structure shows that the species forming and eventually isolated is an octahedral Al(III) complex with three quinic acid moieties coordinated to it. More specifically, the three carboxylate groups of the corresponding ligands along with the three  $\alpha$ -alkoxy moieties bind to Al(III) through formation of five-membered metallacyclic rings. The total charge of the complex is zero. The structure of the complex itself is shown in the ORTEP diagram below (Figure 1).



**Figure 1.** ORTEP diagram of the  $\text{K}[\text{Al}(\text{C}_7\text{H}_{11}\text{O}_6)_3] (\text{OH}) \cdot 5\text{H}_2\text{O}$  complex

Further evidence on the structure of the complex comes from NMR spectroscopy (Figure 2).

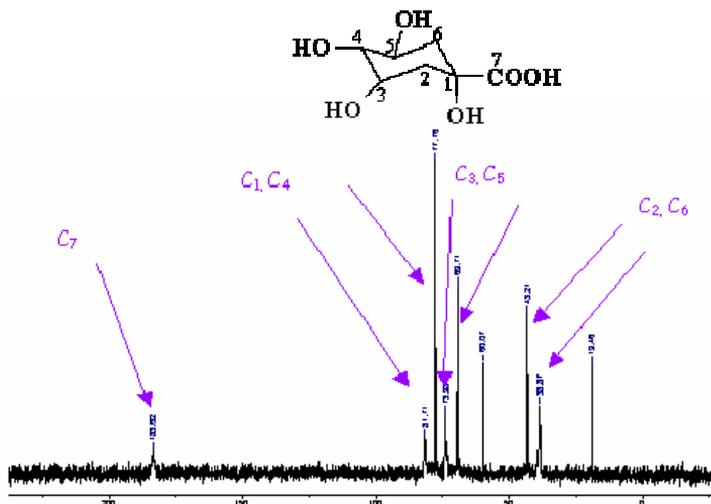


Figure 2.  $^{13}\text{C}$ -NMR spectrum of species **1** in water

## Conclusions

The synthetic efforts developed in the binary aqueous Al(III)-quinic acid system denotes the underlying chemical importance of Al(III) biotoxicity. The structural attributes of the title complex  $\text{K}[\text{Al}(\text{C}_7\text{H}_{11}\text{O}_6)_3](\text{OH}) \cdot 5\text{H}_2\text{O}$  (**1**) exemplifies key attributes of soluble species of Al(III) that might be involved in further potential toxic effects. Especially important is the absence of charge on the complex, which renders the species capable of expediently traversing cellular membranes and concomitantly participating in biological events of potential toxicity. Further work on the system itself through synthetic and solution speciation studies is expected to shed more light in this direction and help in the delineation of Al(III) biotoxicity.

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