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# DISCOVERING THE CONNECTIONS OF THE AQUEOUS CHEMISTRY OF Ti(IV) TO CELLULAR BIOCHEMISTRY. RELEVANCE TO FOOD AND HEALTH

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## Abstract

*The presence of titanium in chemical and biological systems has been amply emphasized over the past decades. The use of that early transition metal in widespread medical and agricultural applications necessitates the perusal of its related chemistry with variable size biological substrates. Keeping in mind that interactions of titanium with cellular components are key to understanding its role in a complex biological world, an in-depth investigation was carried out on the speciation chemistry of the binary Ti(IV)-citric acid system in aqueous media.*
***Key words:*** *titanium, citric acid, structural speciation*

## Introduction

Titanium, a well-known early transition metal, is widely used in various industries. Outstanding applications of titanium include among others the manufacturing and use of whitening agents used in the food and pharmaceutical industry (Stryer, 1997). To that end, as a fairly available metal, titanium has been the target of several studies reported, while numerous assessments have been made on its potential as a candidate food-grade material (Feliciani, 1998). Moreover, its rugged nature has made it an indispensable component of metal alloys employed in surgical rectification devices to remedy malformation or bone-problems in humans (Kuzel, 2003).

Titanium (Ti), beyond the typical uses of metal in various industries, has been reported to exhibit significant biological effects on plants (Alcaraz-Lopez, 2003). These effects could be beneficial at low concentrations and toxic at higher concentrations. In this sense, results

of hydroponic experiments with oats have proposed that hormesis is a major effect exemplifying the mechanism of Ti action in plants. Ti(IV)-ascorbate on the other hand, could be used in mixtures being sprayed on plum trees in several combinations with other commercial compounds containing Ca(II) and Mg(II). The beneficial effects reported in this case were attributed on Ti absorption, translocation and assimilation processes (Lomer, 2002).

In all of the biologically relevant cases, it appears that titanium comes in contact with biological components of low as well as high molecular mass. Without discounting the importance of high molecular mass biotargets in the development of interactions with titanium, low molecular mass substrates, such as the α-hydroxycarboxylic acid citric acid, constitute significant metal ion binders at the cellular level. To investigate the arising interactions of Ti(IV), one of the two most prevalent oxidation states of the metal (III,IV), with citric acid as one such physiological component, helps delineate the requisite biochemical effects and their repercussions to the general health of the organisms and humans involved. To this end, the binary system Ti(IV)-citric acid was studied synthetically, key species were isolated and investigated spectroscopically, structurally and electrochemically (Dakanali, 2003).

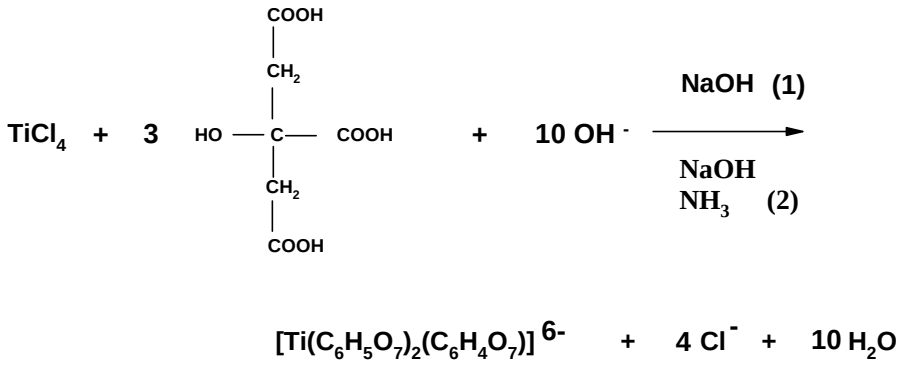
## Experimental

The synthesis and isolation of the two new complexes:

$$Na_6[Ti(C_6H_5O_7)_2(C_6H_4O_7)] \cdot 16H_2O \ (\mathbf{1})$$

$$Na_3(NH_4)_3[Ti(C_6H_5O_7)_2(C_6H_4O_7)] \cdot 8.5H_2O \ (\mathbf{2})$$

was achieved in water under pH specific conditions. Addition of aqueous sodium hydroxide in **1** and equal amounts of aqueous ammonia and sodium hydroxide in **2**, raised the pH of the solution to ~6.0, and concurrently provided the necessary counter ions for the derived anionic complexes. The resulting colorless solutions were treated with ethanol at 4°C and afforded efficiently colorless crystalline materials.




## Results and Discussion

Analytical, spectroscopic and finally X-ray crystallographic studies (Figure 1) revealed the identity of the synthesized species at a near physiological pH value. FT-IR spectroscopy was instrumental in pointing out the coordination of citric acid to the metal ion Ti(IV). Symmetric as well as antisymmetric vibrations for the carboxylate carbonyl groups in the citrate ligands were present in the FT-IR spectra of both complexes **1** and **2** pointing out a change in the coordination environment of citric acid upon reaction with Ti(IV). $^{13}$C-NMR spectroscopy in the solid state was equally informative on the coordination mode of citrate to Ti(IV). In combination with solution $^{13}$C- and $^{1}$H-NMR spectroscopy, significant details were discovered about the solution behavior of the title species in comparison with their structure in the solid state. As a discrete species, complexes **1** and **2** arose out of aqueous media to project a very distinct picture of a) the mode of citrate coordination, b) the degree of protonation of the three citrate ligands around the central metal ion, and c) the concomitantly formulated octahedral geometry around Ti(IV). Most important of all, however, was the variable protonation state of the bound citrate ligands around Ti(IV). Specifically, two of the bound citrates were triply deprotonated, while the third one was fully deprotonated.

Collectively, the synthetic efforts targeting Ti(IV)-citrate complexes from aqueous solutions have contributed significantly in delineating the nature of a number of such species arising in the course of pH-dependent reactions. The structural and spectroscopic data in

the solid state and in solution are in accordance with the picture of mononuclear species of Ti(IV) interacting with citrate in the solution of the synthesis reaction. Furthermore, in solution, the mononuclear octahedral complex **1** in the solid state dissociates in solution to give off free citrate, leaving behind a Ti(IV) species with two citrate ligands. The remaining coordination sites in the environment of the metal ion are occupied by solvent water molecules. Beyond the aforementioned data, cyclic the voltammetry of aqueous solutions of **1** or **2** exhibits a chemically reversible wave, at a $E_{1/2}$ value within the potential range of the Ti(III)/Ti(IV) couple for titanium reagents employed in biochemical and biological experiments.

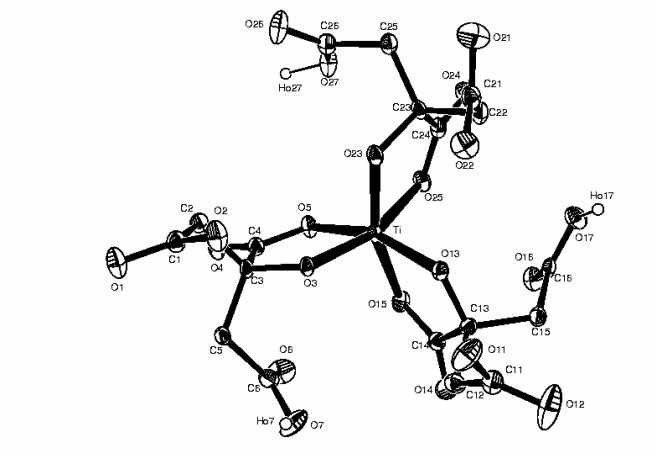



**Fig. 1**. ORTEP diagram of the $[Ti(C_6H_5O_7)_2(C_6H_4O_7)]^{6-}$ anion with the atom labelling scheme in **1**.

## Conclusions

Each well-characterized species from this work reflects the power of the synthetic chemistry in unraveling structurally and spectroscopically characterized Ti(IV)-citrate complexes, thus enabling elucidation of the requisite aqueous distributions prior to any relevant speciation studies. To this end, the contribution of the aqueous synthetic chemistry to the structural speciation of the binary

system Ti(IV)-citrate is significant. Moreover, the structural speciation strategy offers detailed physicochemical information, which would help establish the basis of understanding of potential interactions of Ti(IV) with biologically relevant molecules.

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## References

Alcaraz-Lopez, C., Botia, M., Alcaraz, C.F., Riquelme, F. (2003). Effects of foliar sprays containing calcium, magnesium and titanium on plum (Prunus domesticaL.) fruit quality. *J. Plant Physiol. 160(12)*, 1441-1446.

Dakanali, M., Kefalas, E.T., Raptopoulou, C.P., Terzis, A., Voyiatzis, G., Kyrikou, I., Mavromoustakos, T., Salifoglou, A. (2003). A New Dinuclear Ti(IV)-Peroxo-Citrate Complex from Aqueous Solutions. Synthetic, Structural, and Spectroscopic Studies in Relevance to Aqueous Titanium(IV)-Peroxo-Citrate Speciation. *Inorg. Chem. 42(15)*, 4632-4639.

Feliciani, R., Migliorelli, D., Maggio, A., Gramiccioni, L. (1998). Titanium: a promising new material for food contact. A study of titanium resistance to some aggressive food simulants. *Food Addit. Contam. 15(2)*, 237-242.

Kuzel, S., Hruby, M., Cigler, P., Tlustos, P., Van, P.N. (2003). Mechanism of Physiological Effects of Titanium Leaf Sprays on Plants Grown on Soil. *Biol. Trace Elem. Res. 91(2)*, 179-190.

Lomer, M.C., Thompson, R.P., Powell, J.J. (2002). Fine and ultrafine particles of the diet: influence on the mucosal immune response and association with Crohn's disease. *Proc. Nutr. Soc. 61(1)*, 123-130.

Stryer, L. (1997). Biochemistry. 2η έκδοση, *University Press of Crete, Heraklion, Greece*