# Computational approach to aluminum biochemistry

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In the last century, human intervention has made aluminum highly bioavailable[1]. However, there is increasing evidence that aluminum could be behind of a variety of toxic effects in biological systems, with significant risks for human health. Indeed, aluminum is not involved in any biological cycle and it has been associated with some neurodegenerative diseases, such as the Alzheimer Disease[2].
In this context, the goal of chelation therapy is the removal of toxic metal ions from human body or attenuation of their toxicity by transforming them into less toxic compounds[3].
Such a situation led several groups to focus the attention and to make efforts toward the identification of aluminum-specific chelating agents, with a need to rationalize the effect of different substituents in the modulation of the Al(III)-ligand binding affinity. Accordingly, we think that a computational approach, using *state-of-the-art* theoretical tools, would provide valuable insights toward the development of new powerful aluminum chelators.
In the present work, we have assessed the affinity of aluminum for two families of bidentate chelating agents (salicylic acids and catechols[4]) bearing different substituents, for which rigorous experimental data are available[5]. Binding energies calculated in aqueous solution at the B3LYP-D3(BJ)/6-311++G(3df,2p) level of theory show very good agreement with respect to experimental stability constants, thus validating our theoretical protocol.
Besides, we have characterized geometrical features and different physico-chemical quantities for the Al-O interactions, by means of the Bader's Quantum theory of Atoms in Molecules (QTAIM), Natural Bond Orbital (NBO) theory and the Energy Decomposition Analysis (EDA) scheme by Ziegler and Rauk.
Interestingly, we found that there is a small but significant degree of covalency in these mainly electrostatic closed-shell Al-O interactions, which provides an explanation for the different modulation of the binding affinity by Electron Donating Groups (EDGs, $CH_3$, $OCH_3$) and Electron Withdrawing Groups (EWGs, $NO_2$ and $CF_3$).
The present findings would provide a valuable help in the design and tuning of new, suitable Al(III) chelating agents.

**Acknowledgments:** The authors would like to thank the technical and human support provided by the SGI/IZO (SGIker) of the UPV/EHU. Financial support comes from the European Commission (642294 – TCCM). GDT would like to thank Dr. Joanna I. Lachowicz (University of Cagliari) and Dr. Valerio Di Marco (University of Padua) for valuable insights.

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