Rational Design of Multifunctional Antioxidants

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Abstract

Details on a strategy for computationally designing multifunctional antioxidants is presented. It comprises two stages. The first one involves non-electronic calculations, based on structure-activity relationships. In this stage several parameters are estimated to predict if the designed compounds fulfill the Lipinski's and Ghose's rules for orally active drugs, as well as the Veber criteria. In addition, the potential toxicity of the compounds is evaluated, as well as their synthetic accessibility. Details on the computational tools used for such estimations are provided. The second stage involves electronic calculations, within the frame of the density functional theory. In this stage, the radical-trapping (primary, or type I) and preventive (secondary, or type II) antioxidant capacity is predicted based on thermochemical and kinetic calculations, following the QM-ORSA (quantum mechanics based test for overall free radical scavenging activity) protocol.[1] Details on how to perform such calculations, including environmental effects such as the pH and the diffusion are provided. As an example of application, the rational design of some melatonin derivatives intended to be multifunctional antioxidants, and better to that purpose than the parent molecule, is presented.[2]

1. Annia Galano, Juan Raúl Alvarez-Idaboy "A Computational Methodology for Accurate Predictions of Rate Constants in Solution: Application to the Assessment of Primary Antioxidant Activity" *J. Comput. Chem*. **2013**, *34*, 2430–2445.

2. Annia Galano "Computational-Aided Design of Melatonin Analogues with Outstanding Multifunctional Antioxidant Capacity" *RSC Adv.* **2016**, *6*, 22951–22963.