Theoretical investigation of the conformational space of baicalin.

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Abstract

Flavonoids are a large group of polyphenolic compounds ubiquitously present in plants. They are important components of human diet. They are recognized as potential drug candidates to be used in the treatment and prevention of a lot of pathological disorders, due to their protective effects. Baicalin (7-glucuronic acid 5, 6-dihydroxyflavone) is one of the main single active constituents isolated from the dried roots of Scutellaria baicalensis Georgi. The great interest on this flavonoid is due to its various pharmacological properties, such as antioxidant, antimicrobial, anti-inflammatory, anticancer and so on, and its high accumulation in the roots of S. baicalensis. The aim of our work was to analyze the geometric and electronic properties of baicalin conformers (BCL), thus performing a complete search on the conformational space of this flavonoid in gas phase and in aqueous solution. The results indicate that the conformational space of baicalin is formed by eight conformers in gas phase and five conformers in aqueous solution optimized at B3LYP/6-311++G** theory level. $BCLa2_{TT}$ and $BCLa1_{TT}$ conformers have low stability in gas phase and very high stability in aqueous solution. This variation is related to a modification in the τ_1 angle that represents the relative position of the glucuronide unit respect to the central rings of the flavan nucleus (A and C). This modification was successfully explained by examining the changes in the hydrogen bond (HB) interactions that occur in the region around the hydroxyl group located in position 6 of ring A. Besides, the molecular electrostatic potential (MEP) and frontier molecular orbital (FMO) analyses indicate that $BCLa2_{TT}$ and $BCLa1_{TT}$ conformers are the most favorable conformers for interacting with positively charged species (such as metal ions) in aqueous media (such as biological fluids).