Investigation Of The Structure Of Celecoxib Molecule And Its Interaction With Cox-2 By Quantum Mechanical Methods Using Model Systems

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Non-steroidal anti-inflammatory drugs (NSAID) inhibit the eventual conversion of COXs to metabolites of arachidonic acid, including prostaglandins, prostacyclin, and thromboxanes, in the immune response after injury or infection. Selective COX-2 inhibitors (coxibs), a subset of NSAIDs, act specifically on the COX-2 enzyme. One of the coxibs, celecoxib, is marketed under the brand name Celebrex. Celebrex is a non-steroidal anti-inflammatory drug that exhibits anti-inflammatory, analgesic and antipyretic activities. Like other coxibs, it inhibits prostaglandin synthesis and thus reduces inflammation, which are mediators of fever and pain. It is the only coxib currently available in the United States. In this study, the structure of Celebrex will be investigated by quantum mechanical methods and its interaction with amino acids in the COX-2 inhibition mechanism will be examined with the same approach through the amino acid arginine. For this, firstly, conformational analysis of Celebrex was performed by using Spartan18 with molecular mechanics. By using the density functional theory (DFT) method for selected conformers, optimization and frequency calculation were carried out with Gaussian16 at ωB97XD/6-311++G(d,p) level mimicking the solvent as water. Relative energies were used to select the most stable conformers for each molecule. Molecular structures were displayed using Discovery Studio Visualizer 2019 program. A similar workflow was applied for arginine. The interactions of the most stable celecoxib and arginine structures were investigated at the same DFT level using the structures formed using Spartan18. It is thought that the results obtained from the calculations can help clinical studies in elucidating the working mechanism of Celebrex and contribute to the design of similar molecules with less side effects.