Ab Initio and Molecular Modeling Study of the Interaction of Flavonoids with Human Serum Albumin Validated by Fluorescence Spectroscopy

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Flavonoids are a large class of naturally occurring polyphenols widely distributed in plants, which exhibit some pharmacological activities like antibacterial and antioxidant. The interaction between Rutin (Ru) and Guaijaverin (Gua) flavonoids and Human Serum Albumin (HSA) was investigated by *ab initio* and molecular modeling calculation with the validation of theoretical calculations performed by fluorescence spectroscopy. The structure of the flavonoids utilized in the molecular modeling calculation was obtained by Gaussian program series 98. The optimization geometry of flavonoids were performed in its ground state by using *ab initio* DFT/B3LYP functional with a 6-31G(d,p) basis set used in calculations. HOMO-LUMO energy gap of Ru (3.96 eV) and Gua (3.81 eV) were determined and converted into wavelength (313 and 326 nm, respectively) falling exactly into the overlap spectral region between Trp214 fluorescence and absorbance spectra of flavonoids. Such results combined with the quenching efficiency of Trp214 fluorescence by flavonoids are crucial to validate the molecular modeling tools performed by AutoDock 4.2 program. Therefore details of the binding site for flavonoids were described within the hydrophobic pocket of the subdomain IIA of HSA. The best energy ranked result shows that Ru (-24.5 kJmol⁻¹) and Gua (-29.3 kJmol⁻¹) are localized in the proximity of the single tryptophan residue Trp214 and the distances r = 2.40 and 2.53 nm, respectively, between the donor (HSA-Trp214) and the acceptor (flavonoids) obtained by means of fluorescence resonance energy transfer (FRET) confirms its localization. The arrangement of amino acid residues around the flavonoids obtained by molecular modeling shows that interaction is not exclusively hydrophobic in nature, since there are polar residues that are responsible for hydrogen bonds and electrostatic interactions what is confirmed by thermodynamic parameters ΔH, ΔS, and ΔG.

Keywords: Flavonoids, Human Serum Albumin, *Ab Initio*, Molecular Modeling, Fluorescence Spectroscopy

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