ABSTRACT

Glycation is a non-enzymatic reaction between proteins, nucleic acids, or lipids and reducing sugars, forming end products known as advanced glycation end products (AGEs). Glycation disrupts protein function because this reaction can alter the 3-dimensional conformation of the protein. Glucose and fructose have been reported to interact with Human Serum Albumin (HSA) in vitro and in silico. Previous in vitro studies have proven that this interaction causes the glucose and fructose rings to open when interacting with Lys-199 and results in covalent bonding with Lys-195 and glucose. Previous in silico research reported that Lys-199 and Lys-195 are the strongest interaction sites when interacting with linear glucose. This research, however, was general and conducted across the entire HSA protein, thus not specifically explaining the interactions occurring at Lys-199 and Lys-195.

The aim of this study is to more accurately predict the initial interactions in glycation reactions based on bond distance parameters, interaction energy, UV spectra, and molecular orbitals. The study utilizes HSA protein with PDB code 4IW2 as the receptor. Both cyclic and linear structures of glucose and fructose were used as ligands. The study was conducted using molecular docking methods to obtain the optimal interaction position between the receptor and ligand using PyRx 1.17.1 software. The results were then used for quantum mechanics calculations. The quantum mechanics method employed was density functional theory (DFT) with a B3LYP/6-31g(dp) basis set, and time-dependent functional theory (TDDFT). Quantum mechanics calculations were conducted with the aim of optimizing molecular structures, obtaining molecular orbitals, and UV spectra of complexes between LK199C (Leu-Lys199-Cys) and AK195Q (Ala-Lys195-Glu) with glucose and fructose. Analysis and visualization were performed using Chimera 1.11.2 and Chemcraft 1.8 software.

The results of this study indicate that LK199C is predicted to have a higher potential for interacting with cyclic glucose, as shown by the LK199C...Cyclic Glucose complex having the most negative interaction energy at -43.259 kJ/mol, and the formation of two hydrogen bonds between them. AK195Q is predicted to have a higher potential for interacting with linear glucose, as indicated by the AK195Q...Linear Glucose complex having the most negative interaction energy at -44.283 kJ/mol, along with a UV spectral shift depicting conformational changes in the receptor due to the strong interaction between the receptor and ligand.

Keywords: Glycation reaction, HSA protein, Glucose, Fructose, Quantum mechanics