ABSTRACT - APPLICATIONS OF BIOTECHNOLOGY IN HUMAN HEALTH (VACCINE AND DRUG DEVELOPMENT);

ANTIGLYCANT POTENTIAL AND PROTECTIVE EFFECTS OF PICEATANNOL ON HUMAN HEMOGLOBIN: STRUCTURAL AND THERMODYNAMIC INSIGHTS

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Piceatannol (PIC) is a stilbene compound structurally analogous to resveratrol and belongs to a broad group of natural defense polyphenols found in various plant species, such as grapes, blueberries, and sugarcane. It is a major bioactive constituent of yellow passion fruit (Passiflora edulis) seeds, exhibiting antioxidant, antiglycation, and fibrillation-inhibitory activities, particularly relevant against degenerative and metabolic disorders such as Alzheimer's disease and diabetes. One of the key biochemical pathways leading to these conditions is the formation of advanced glycation end products (AGEs) through non-enzymatic reactions, such as the Maillard reaction, between reducing sugars

and nucleophilic groups of biomolecules. As such, the objective of this work was to obtain the progression or decrease of Hb's glycation, through the measurement of AGEs fluorescent, by analysis of the structural changes in the Soret band of Hb, by the formation of Hb aggregates, in the presence of PIC (10 – 300 μM) and using glucose and glucose-fructose mixture as reducing sugars in the process, performed over a period of 5 weeks. Additionally, Hb–PIC interactions were characterized by fluorescence spectroscopy at different temperatures (298, 304, and 310 K), and molecular docking simulations were performed to predict binding modes and affinities. As a result, PIC inhibited Hb glycation by 88% and 81% when Hb was incubated with glucose and with a glucose–fructose mixture, respectively, at a concentration of 300 μM. Analysis of the Soret band and ThT fluorescence revealed clear protective effects of PIC against alterations in the Hb heme group and the formation of amyloid fibrils. PIC prevented heme alterations by up to 23% and reduced amyloid fibril formation by up to 52%, underscoring its ability to counteract glycation-induced conformational damage. Thermodynamic analysis revealed a spontaneous interaction between PIC and Hb (ΔG = –24.04 kJ.mol^{-1}), supported by docking predictions indicating a favorable binding free energy (–27 kJ.mol^{-1}) primarily driven by electrostatic interactions. According to these results, indicate that PIC effectively inhibits protein glycation, preserves hemoglobin structure, and limits amyloid fibrillation, suggesting its potential as a therapeutic agent for preventing glycation-associated complications, especially those related to diabetes and neurodegenerative diseases.

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Palavras-chave: hemoglobin; antiglycation; piceatannol; soret; tht; ages.