Mehran Miroliaei, J Glycobiol 2018, Volume 7
DOI: 10.4172/2168-958X-C2-015

Chlorogenic acid and curcumin reduce the impact of global glycation damage in human hemoglobin

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The molecular mechanism by which natural phenolics can delay or reduce glycation-induced protein cross-linking is a subject with little attention in biomedicine. The present work investigates the modus operandi of chlorogenic acid (CGA) and curcumin (CUR), in inhibiting fructose-derived advanced glycation end products (AGEs) and AGE-protein cross-links in human hemoglobin (Hb). The two ligands protected Hb by inhibiting the increase in cross-β structure in a concentration dependent fashion. Upon the occurrence of AGE, the two ligands were found to influence the amyloid aggregation at different stages of intermediate structure formation, ability determined by ThT fluorescence and Congo red assay. Ligand treatment appreciably protected "heme" degradation in the early phase of glycation by arresting the conformational changes at the secondary structure element of the protein. Upon addition of the ligands, glycated-Hb adopts fewer surface hydrophobicity and β-sheet content evidenced by ANS fluorescence and far-UV CD, respectively. Meanwhile, CGA and to a lesser extent CUR lessened the modification of thiol and lysine residues more efficiently than aminoguanidine. Considerable prevention by CGA in the Soret region of the spectra of glycated Hb was also noticed. Accordingly, chaperone-like property is proposed for the ligands by which the exposed hydrophobic surface of the glycated Hb, as the driving force for aggregation, was deteriorated. Molecular docking studies and hydrophobic probe (ANS) displacement revealed that the ligands bind within the hydrophobic pocket of Hb. We conclude that the remarkable inhibitory effects of the ligands come from hampering the cross-β structure pathway in which globular Hb turns into amyloid cross-link. These properties would offer CGA as a potential therapeutic approach to combat the pathological cross-link formation associated with glycation.

Biography

Mehran Miroliaei has completed his PhD in Biochemistry from the Institute of Biochemistry and Biophysics (IBB), University of Tehran. Presently he is a Lecturer at the University of Isfahan. He has published more than 35 papers in reputed journals and has been serving as an Editorial Board Member of repute.

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