Bio-Physical characterization of Ribose Induced DNA Glycation: A study on structural perturbation of DNA macromolecule

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Abstract

The non enzymatic attachment of carbonyl group of sugar moiety to the amino group of macromolecule non enzymatically leads to the formation of early glycation products (Amadori products) which further undergoes rearrangement, cyclization and dehydration to form advanced glycation end products (AGEs). AGEs trigger proinflammatory, profibrotic and procoagulant cellular responses that are capable of damaging tissues or targeting particular organs, play a significant role in the pathophysiology of various disease like diabetes, atherosclerosis, cataract formation, renal dysfunction and Alzheimer’s disease. While the formation of glucose glycated DNA was previously demonstrated, no extensive studies have been performed to assess D-ribose induced glycation of calf thymus DNA. D-Ribose an important monosaccharide, is highly active (several folds than glucose) in the glycation reaction, and results in the rapid production of AGEs. The present study was initially designed to investigate the non enzymatic glycation of calf thymus DNA by using different concentrations of D-ribose at increasing time period (1-21 days). The obtained AGEs were characterized with respect to the extent of DNA strand break and base modifications. Additionally, their absorbance, agarose gel electrophoresis, fluorescence, circular dichroism (CD) and thermal denaturation (Tm) characteristics were also extensively studied. Our results demonstrated that glycated DNA showed significant differences in the degree of modification and in AGE-specific fluorescence using different concentration of modifiers (D-ribose). The results provide the mechanistic insight of D-ribose induced glycation in calf thymus DNA and also suggest significant conformational changes within the glycated DNA. In this study we propose a set of parameters that is sufficient to partially characterize AGEs used for biochemical studies.

Keywords: Amadori products; Advance glycation end products; AGEs characterization; DNA strand modification.

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