

Methylglyoxal Induced Glycooxidation of Human Low Density Lipoprotein: A Biophysical Perspective and Its Role in Diabetes and Periodontitis

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Abstract : Diabetes mellitus (DM) induced metabolic abnormalities causes oxidative stress which leads to the pathogenesis of complications associated with diabetes like retinopathy, nephropathy periodontitis etc. Combination of glycation and oxidation 'glycooxidation' occurs when oxidative reactions affect the early state of glycation products. Low density lipoprotein (LDL) is prone to glycooxidative attack by sugars and methylglyoxal (MGO) being a strong glycating agent may have severe impact on its structure and consequent role in diabetes. Pro-inflammatory cytokines like IL1 β and TNF α produced by the action of gram negative bacteria in periodontitis (PD) can in turn lead to insulin resistance. This work discusses modifications to LDL as a result of glycooxidation. The changes in the protein molecule have been characterized by various physicochemical techniques and the immunogenicity of the modified molecules was also evaluated as they presented neo-epitopes. Binding of antibodies present in diabetes patients to the native and glycated LDL has been evaluated. Role of modified epitopes in the generation of antibodies in diabetes and periodontitis has been discussed. The structural perturbations induced in LDL were analyzed by UV-Vis, fluorescence, circular dichroism and FTIR spectroscopy, molecular docking studies, thermal denaturation studies, Thioflavin T assay, isothermal titration calorimetry, comet assay. MALDI-TOF, ketoamine moieties, carbonyl content and HMF content were also quantitated in native and glycated LDL. IL1 β and TNF α levels were also measured in the type 2 DM and PD patients. We report increased carbonyl content, ketoamine moieties and HMF content in glycated LDL as compared to native analogue. The results substantiate that in hyperglycemic state MGO modification of LDL causes structural perturbations making the protein antigenic which could obstruct normal physiological functions and might contribute in the development of secondary complications in diabetic patients like periodontitis.

Keywords : advanced glycation end products, diabetes mellitus, glycation, glycooxidation, low density lipoprotein, periodontitis

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