Abstract

Diabetes is the most common metabolic disorder affecting millions of people all over the world. It is a group of disorders and a major risk factor for cardiovascular diseases. The common underlying mechanism linking all these is the high blood glucose level. High glucose in the blood can become toxic to the cells and tissues by many mechanisms. One of the mechanisms is formation of non-enzymatic glycation end products (AGE). Glucose in the open chain form can react with amino group of proteins forming an Amadori product which undergoes rearrangement to form stable glycation products. Theses glycation products can affect the function of proteins and hence are responsible for diverse diseases.

In this study we have investigated the glycation of HDL by glyoxal and glucose. In-vitro glycation was monitored by the loss of paraoxonase (PON) activity in a dose and time dependent manner. At high glucose concentration there was reduced loss of PON activity. Glyoxal and glucose were both able to modify amino groups and thiol groups. Glycation resulted in decrease in the arylesterase activity but increase in paraoxonase when the serum was passed through cibacron blue sepharose column. Glycation also increased AGE formation in HDL as well as endothelial cells of the human umbilical vein. The glycated ApoA1 was antigenic and was able to produce antibodies in rabbits and hen. However the rabbit antibody was more specific than the hen antibody.

When the rabbit antibody was used to quantitatively estimate the amount glycated HDL in diabetic subjects, there was no significant difference between control and diabetics. However HbA1c levels correlated with glycated HDL. At relatively lower concentration of HDL, there was no effect on glycation, but at higher concentration of HDL glycation decreased. HbA1c did not correlate with PON or arylesterase activity. Also HbA1c was not dependent on the Hb levels but on the duration of diabetes. Females had more HbA1c than males.

Our results show that HDL is susceptible to glycate modification. Glycated HDL had modified paraoxonase activity against different substrates. However at higher level of glycation all the enzyme activities decreased and there was an increase in AGE formation. Thus glycation of HDL in diabetes can be a cause of loss of anti-atherogenic activities of HDL.