

Letter to the Editor

The liver cell histones of diabetic patients contain glycation endproducts (AGEs) which may be lipofuscin components

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One of the consequences of sustained hyperglycaemia in diabetes mellitus (DM) is the glycation of proteins. In this mechanism the initial reaction is condensation of glucose with the ϵ -amino groups of proteins, forming the Amadori adduct of fructoselysine. This may further react by initiating a complex series of reactions leading to accumulation of a yellow-brown, fluorescent Maillard's advanced glycation endproduct (AGE) [1]. Earlier, we reported on the glycation of histone proteins (glycohistones) and, later, on liver cell histones of diabetic individuals, which are also intranuclearly glycated by the initial Amadori reaction [2].

We have now examined, in two experiments, whether AGEs could be detected in liver cell histones of diabetic individuals.

In the first experiment, we incubated liver slices of nondiabetic individuals and 5 mg albumin separately with 30 mmol/l glucose (pH 8.9) at 37°C for 1 week. Both the liver slices and the albumin turned yellow. This colour was

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strongly reminiscent of lipofuscin, appearing on the protein structures paraffin wax slides of liver cells. The excitation maxima of the fluorescence spectrum of the albumin solution and the incubation solution of the yellow liver slices were 370 nm, and that of emission was 435 nm [3], which was characteristic of AGEs and also of lipofuscin.

In a second experiment, total histones obtained from liver cell nuclei of 3 patients with Type 1 DM and 3 with Type II DM were isolated [4]. Their clinical data was: age, 52–68; duration of DM, 12–21 years; fasting blood glucose, 9.8–17.2 mmol/l; serum creatinine, 251–610 μ mol/l. Eight age-matched, nondiabetic individuals with hypertension served as controls.

An analysis of the AGEs was done using their characteristic fluorescence spectra which gave the results described above. In the diabetic individuals, total AGE-linked fluorescence (in arbitrary units) was twice as high as in the controls: 18.7 ± 5.1 versus 7.3 ± 2.2 . This agrees with what has been seen in experimental DM [5].

Our data suggest that in DM, not only early but also late, histone glycation occurs and forms what is termed AGEs. On the other hand, on the basis of the close similarity between the fluorescence spectra of the yellow pigments, we assume that, besides lipid derivatives [1], AGEs are the main components of lipofuscin.

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