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The role of oxidative stress on protein glycation

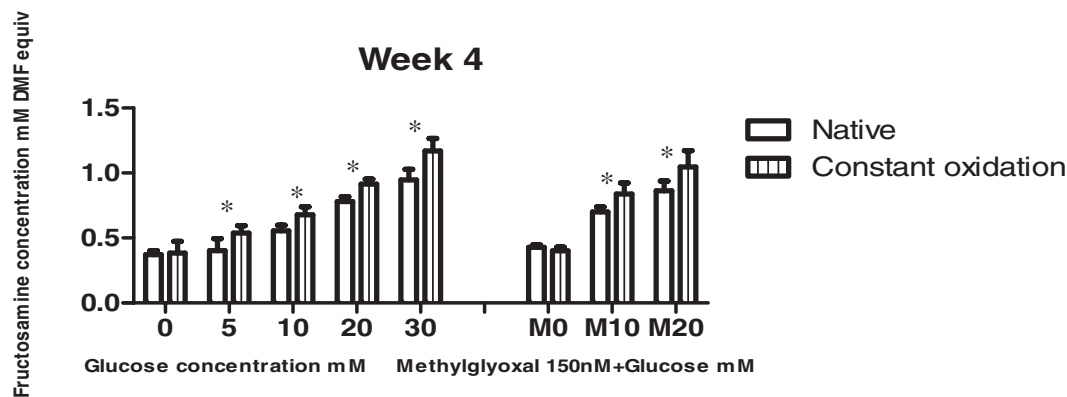
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Protein glycation is a major cause of tissue damage in patients with diabetes. Commonly believed to be associated with increased blood glucose, glycated proteins are in fact found in normoglycaemic individuals. Cross-sectional studies have observed a negative association between fruit and vegetable consumption and protein glycation in diabetic individuals⁽¹⁾. Based on these results, a variety of studies have attempted to attribute a protective role to various dietary antioxidants, polyphenols and foodstuff against glycation. The majority of these studies involve *in-vitro* experiments and hence so far the scientific results on this area have been treated cautiously^(2,3). A closer look to the experimental conditions and results available in the literature highlighted that the amount of protein damage *in vitro* is smaller than observed in cross-sectional studies, raising questions regarding the pathophysiological mechanism involved. In this study, we aimed at identifying the potential effect of oxidation in the glycation process.

Albumin (40 g/L) was incubated with physiological levels of glucose (0–30 mM) with or without methylglyoxal (150 nM) for 4 weeks. To investigate the effect of oxidation on protein glycation, albumin was used as native or pre-oxidized (either for 8 hours prior to glycation with 10 nM H₂O₂, or throughout the incubation period). Fructosamine (with nitroblue tetrazolium) and fluorescence were measured at two and four weeks. All incubations took place under sterile conditions (sodium azide, 0.2 g/L) and in six true replicates, while all measurements were duplicated.

Protein oxidation both prior or during glucose exposure statistically promoted protein glycation with all glucose levels tested. Moreover, only oxidized protein was significantly glycated at physiological glucose levels (5 mM) compared to native albumin ($p = 0.001$, Figure 1). Oxidized albumin was also glycated in 10 mM glucose compared to native albumin (significant increase at 2 rather than 4 weeks).



* $p < 0.05$ native vs constant oxidation

Figure 1: Fructosamine concentration at week 4 during constant exposure to oxidation.

The first stages of protein glycation leading to fructosamine production are believed to be dependant on glucose concentration, as opposed to the later stages, driven by both oxidation and glucose concentration. We showed that oxidation is important throughout the glycation process, supporting the view that, *in vivo*, it is glycooxidation rather than glycation that takes place. These findings supports the investigation of the role for foodstuff with antioxidant capacities can in the management of diabetes.

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2. Verzelloni E, Pellacani C, Tagliazucchi D, Tagliaferri S, Calani L, Costa LG *et al.* (2011) *Mol Nut Food Res* **55**, S35–43.
3. Fukino Y, Ikeda A, Maruyama K, Aoki N, Okubo T & Iso H (2008) *EJCN* **62**, 953–60.