

**P014** The role of metal ions in the toxicity of the amylin peptide implicated in type-2 diabetes mellitus and the protective effects of antioxidants and metal ion chelators

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Amyloid deposits derived from a peptide called amylin are found in the pancreas in the vast majority of cases of type 2 diabetes mellitus (T2DM). There is some evidence that pancreatic amylin deposition is associated with oxidative stress and it has also been reported that diabetic patients have defects in antioxidant protection mechanisms and impaired trace element metabolism. However, the mechanism of toxicity of amylin is still not clear. We have recently reported that the human amylin peptide generates hydrogen peroxide *in vitro* during its aggregation into amyloid fibrils and that this process is greatly stimulated by Cu(II) ions. For the study reported here, cell toxicity assays employing RINmf5 cells were used to assess the effects of metal ions on amylin toxicity and to test antioxidants and metal ion chelators for their protective effects against the oxidative stress generated through amylin aggregation. We found that only Cu(II) ions markedly potentiated the cytotoxicity of amylin, and protective effects were found using several synthetic antioxidants and copper ion chelators (carnosine,  $\alpha$ -lipoic acid, trientine and thiazolidinediones) as well as with catalase. Our data provide a new rationale and added impetus for the clinical use of antioxidants and copper chelators in T2DM.