Development and application of a stable isotope dilution analysis for the quantitation of advanced glycation end products of creatinine in biofluids of type 2 diabetic patients and healthy volunteers.

Abstract:
N-(1-Methyl-4-oxoimidazolidin-2-ylidene) ?-amino acids were recently identified in roasted meat as so far unknown advanced glycation end products (AGEs) of creatinine. For the first time, this paper reports on the preparation of (13)C-labeled twin molecules of six N-(1-methyl-4-oxoimidazolidin-2-ylidene) ?-amino acids and the development of a stable isotope dilution analysis (SIDA) for their simultaneous quantitation in meat, plasma, and urine samples by means of HPLC-MS/MS. Method validation demonstrated good precision (<14% RSD) and accuracy (97-118%) for all analytes and a lower limit of quantitation of 1 pg injected onto the column. The SIDA was applied to monitor plasma appearance and urinary excretion of these AGEs in type 2 diabetes mellitus patients (DM, n = 7) and healthy controls (n = 10) prior to and after ingestion of a bolus of processed beef meat. Interestingly, the basal concentration of N-(1-methyl-4-oxoimidazolidin-2-ylidene) aminopropionic acid was elevated in plasma and urine of DM patients compared to healthy individuals. Further, ingestion of processed meat led to a significantly higher concentration of this AGE in biofluids from DM patients when compared to healthy controls. These findings suggest a favored in vivo formation, as demonstrated by physiological model
incubations of creatinine and carbohydrates (37 °C, pH 7.4), or a more efficient dietary up-take of
N-(1-methyl-4-oxoimidazolidin-2-ylidene) ?-amino acids in hyperglycemic diabetes patients.