

## Publication

A 4-week high-AGE diet does not impair glucose metabolism and vascular function in obese individuals.

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**Author(s)** Linkens, Armand Ma; Houben, Alfons Jhm; Niessen, Petra M; Wijckmans, Nicole Eg; de Goei, Erica Ec; Van den Eynde, Mathias Dg; Scheijen, Jean Ljm; van den Waarenburg, Marjo Ph; Mari, Andrea; Berendschot, Tos Tjm; Streese, Lukas; Hanssen, Henner; van Dongen, Martien Cjm; van Gool, Christel Cjaw; Stehouwer, Coen DA; Eussen, Simone Jmp; Schalkwijk, Casper G

Author(s) at UniBasel Streese, Lukas ; Hanssen, Henner ;

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BACKGROUNDAccumulation of advanced glycation endproducts (AGEs) may contribute to the pathophysiology of type 2 diabetes and its vascular complications. AGEs are widely present in food, but whether restricting AGE intake improves risk factors for type 2 diabetes and vascular dysfunction is controversial.METHODSAbdominally obese but otherwise healthy individuals were randomly assigned to a specifically designed 4-week diet low or high in AGEs in a double-blind, parallel design. Insulin sensitivity, secretion, and clearance were assessed by a combined hyperinsulinemic-euglycemic and hyperglycemic clamp. Micro- and macrovascular function, inflammation, and lipid profiles were assessed by state-of-the-art in vivo measurements and biomarkers. Specific urinary and plasma AGEs N*ε*-(carboxymethyl)lysine (CML), N $\varepsilon$ -(1-carboxyethyl)lysine (CEL), and N $\delta$ -(5-hydro-5-methyl-4-imidazolon-2-yl)-ornithine (MG-H1) were assessed by mass spectrometry.RESULTSIn 73 individuals (22 males, mean s SD age and BMI 52 ś 14 years, 30.6 ś 4.0 kg/m2), intake of CML, CEL, and MG-H1 differed 2.7-, 5.3-, and 3.7-fold between the low- and high-AGE diets, leading to corresponding changes of these AGEs in urine and plasma. Despite this, there was no difference in insulin sensitivity, secretion, or clearance; micro- and macrovascular function; overall inflammation; or lipid profile between the low and high dietary AGE groups (for all treatment effects, P >0.05).CONCLUSIONThis comprehensive RCT demonstrates very limited biological consequences of a 4-week diet low or high in AGEs in abdominally obese individuals.TRIAL REGISTRA-TIONClinicaltrials.gov, NCT03866343; trialregister.nl, NTR7594.FUNDINGDiabetesfonds and ZonMw.

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