Advanced glycation end products (AGEs) in metabolic disease: linking diet, inflammation and microbiota

Giulia Gaudioso[1], Debora Collotta[2], Fausto Chiazza[2], Raffaella Mastrocola[2], Alessia Cento[2], Francesca Fava[1], Manuela Aragno[2], Massimo Collino[2], Kieran Tuohy[1]
[1]Fondazione Edmund Mach, San Michele all'Adige, Italy. [2]University of Turin, Turin, Italy

Abstract

Introduction: High sugar consumption promotes endogenous formation of advanced glycation end-products (AGEs), a heterogeneous class of molecules originated from non-enzymatic glycation between reducing sugars and free amino groups of proteins, nucleic acids, or lipids. AGEs accumulation in tissues has been linked to aging and diabetes complications. AGEs might also play an independent role in inflammation and development of cardiovascular disease (CVD). Exogenous dietary AGEs, due to excess intake of modern heat-treated foods, might act synergistically with endogenous AGEs, thus contributing to increase inflammation and CVD. A large amount of ingested AGEs reaches the colon, where they might affect gut microbial metabolism, for example, by acting as substrate for colonic bacterial fermentation, driving alterations of microbiota composition and of intestinal permeability. However in vitro and in vivo studies (animal and human) on the impact of AGEs on the gut microbiota are discordant. This study on mice aims to link the modulation of gut microbiota by AGEs-enriched diet (AGE-D) with metabolic and inflammatory markers.

Materials and methods: C57BL/6 mice were randomly allocated into the following dietary regimens: Control (n=24) and AGE-D (n=20) for 22 weeks. AGE-D was prepared replacing casein (200 g/kg diet) by an equal amount of modified casein where 10% of arginine was glycated with MG-H1 (methylglyoxal 5-hydro-5-methylimidazolone) for a total of 4 μmol of MG-H1 per g of diet. Faeces were collected using metabolic cages (18 h starving) at week 0, 11 and 22 for fecal DNA extraction and 16SrRNA analysis through Illumina MiSeq using V3-V4 targeted primers. After 22 weeks of dietary manipulation, mice were sacrificed, plasma and organ lipid profiles and serum metabolic and inflammatory profiles were determined.

Results and discussion: AGE-D caused a significant reduction in the blood levels of two important components of the incretin system, GIP and GLP-1, when compared to control diet, suggestive of unbalance in the incretin-insulin axis. AGE-D exposure was associated with a significant increase in systemic concentrations of inflammatory cytokines, e.g. IL-1β and IL-17, and PAI-1, which has been suggested as both reliable marker and critical mediator of cellular senescence. We will present how AGEs impact on microbiome community structure and correlate changes in gut microbiota with GIP and GLP-1 levels.

Conclusions: AGEs, characteristic of modern processed foods, appear to impact on the incretin-insulin axis, a key regulator of metabolic disease risk. Diets rich in AGEs may mediate these physiological effects at least in part, by reshaping intestinal microbiota structure.

Conflict of Interest

There is not conflict of interest