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The "form" makes the difference: Unrevealing the differential susceptibility to sugar-induced metabolic derangements evoked by liquid and solid fructose formulations

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Fructose produces 10 times more advanced glycation end products (AGEs) than glucose. We had recently demonstrated that the high chemical reactivity of fructose contributes to the massive formation of intracellular AGEs, thus evoking marked cellular alterations and organ dysfunction. Here, we investigated whether not only the type (e.g. fructose vs. glucose), but also the form (liquid vs. solid) of sugars may affect the development of metabolic impairments. Male C57Bl/6j mice were fed a standard diet (SD), a standard diet plus 60% fructose syrup (L-Fr), or a 60% fructose solid diet plus water (S-Fr), for 12 weeks. Liver lipogenesis, fibrosis, and inflammation, as well as intestinal absorption, accumulation of AGEs, and integrity were assessed by WB, immunofluorescence and histology. Gut microbiota population was characterized by metagenomic sequencing. L-Fr intake induced higher levels of hepatosteatosis associated to a greater expression/activation of the lipogenic SCAP/SREBP signaling pathway and fibrogenic markers in the liver than the S-Fr administration. In contrast, S-Fr evoked in the ileum intestinal mucosa a stronger local AGEs accumulation, RAGE expression, and gut barrier injury, leading to higher concentration of LPS in the portal plasma. The S-Fr related impairment of gut integrity was associated to a stronger activation of the LPS-dependent pro-inflammatory pathway NLRP3 inflammasome in the liver of S-Fr mice than L-Fr mice. Interestingly, the local accumulation of fructose in the intestine led to alterations of the gut microbiota depending on the fructose formulation. Overall, these results convincingly showed that the consumption of different fructose formulations, liquid or solid, may evoke different impact on gut integrity, thus differently affecting liver homeostasis. Our data suggest that, the solid fructose formulation is more slowly absorbed by enterocytes than liquid fructose, thus producing AGEs, leading to systemic inflammation.

Biography

Collino M is a Professor of Pharmacology and Toxicology in the Department of Drug Science and Technology at University of Turin (Italy). He is author of 86 full papers published in international journals with high impact factor; total citations: 1886; h-index: 25. He is the European Coordinator of the European Project "Innovative technological approaches for validation of salivary AGEs as novel biomarkers in evaluation of risk factors for diet-related diseases".

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