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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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Introduction:
Fructose produces 10 times more Advanced Glycation End Products (AGEs), than glucose. We 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 [1, 2]. 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.

Methods:
Male (C57Bl/6) 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 intestinal absorption, accumulation of AGEs, and integrity were assessed by WB, immunofluorescence and histology. Gut microbiota population was characterized by metagenomic sequencing.

Results:
L-Fr intake induced higher levels of hepatosteatosis (liver TG: +80% vs. SD, +33% vs. S-Fr, p<0.05) 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 (+300% vs. SD, +210% vs. L-Fr, p<0.05). 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, with increase in the saccharides metabolizing Lactobacillus genus in the L-Fr, and increased colonization by populations related to intestinal inflammation and barrier disruption, such as Clostridium, in the S-Fr group.

Conclusions:
Overall, these results convincingly show that 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.

References