The gut shields the liver from fructose-induced damage

29 June 2020

After one consumes food or a beverage containing fructose, the gastrointestinal system, or gut, helps to shield the liver from damage by breaking down the sugar before it reaches the liver, according to a new multi-center study led by researchers in the Perelman School of Medicine at the University of Pennsylvania. However, the consumption of too much fructose—particularly in a short period of time—can overwhelm the gut, causing fructose to 'spill over' into the liver, where it wreaks havoc and causes fatty liver, researchers discovered.

Studies have shown that the excessive consumption of fructose can be toxic to the liver. When large quantities of fructose reach the liver, the liver uses excess fructose to create fat, a process called lipogenesis. Eventually, people who consume too much fructose can develop nonalcoholic fatty liver disease, a condition in which too much fat is stored in the liver cells.

Until now, it hasn't been clear whether the gut's role in processing the fructose prevents or contributes to fructose-induced lipogenesis and the development of liver diseases. For this study, the team of researchers, including Princeton University's Joshua Rabinowitz, MD, Ph.D., studied a key enzyme, called ketohexokinase, that controls how fast fructose is consumed. They showed, by genetically engineering mice, that lowering the levels of this enzyme in the gut led to fatty livers in the mice. Conversely, the team showed that increasing the level of ketohexokinase in the gut protected from fatty liver. Thus, the researchers found the breakdown of fructose in the gut mitigates the development of extra fat in liver cells in mice. They discovered that the rate at which the intestine can clear fructose determines the rate at which fructose can be safely ingested.

In addition, the team showed the same amount of fructose is more likely to result in the development
of fatty liver when its consumed via a beverage versus food. Similarly, one faces an increased likelihood of developing fatty liver when consuming fructose in a single setting compared to several doses spread over 45 minutes.

"Collectively, our findings show fructose induces lipogenesis when the intake rate exceeds the gut's capacity to process fructose and protect the liver," Arany said. "In the modern context of excessive availability and consumption of processed foods, it is easy to see how the resulting fructose spillover would drive metabolic syndrome."

**More information:** Cholsoon Jang et al. The small intestine shields the liver from fructose-induced steatosis, *Nature Metabolism* (2020). [DOI: 10.1038/s42255-020-0222-9](https://doi.org/10.1038/s42255-020-0222-9)

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