

Zero-calorie sweeteners on trial again

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As a sugar substitute, zero-calorie sweeteners may reduce tooth decay and blood sugar spikes. Seven are approved worldwide and safe for

humans—but does this mean they're healthy?

For the first time, scientists exposed pregnant and lactating mice to sucralose and acesulfame-K—a common combination in soda, sports supplements and other sweetened products—and found their pups developed harmful metabolic and gut bacteria changes.

Published in *Frontiers in Microbiology*, the study reinforces an emerging consensus: [artificial sweeteners](#) may be safe when used in moderation by adults, but they are not a "magic bullet" alternative to sugar.

The problem with sweeteners

"Non-nutritive sweeteners are generally believed to be safe when used in moderation," says Dr. John Hanover, a glycobiologist and senior author of the study at the U.S. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health. Hanover collaborated with Dr. Stephanie Olivier-Van Stichelen, formerly at NIDDK and now Assistant Professor at Medical College of Wisconsin, and Dr. Kristina Rother, Chief of the Section on Pediatric Diabetes and Metabolism at NIDDK.

"However, sweetness itself seems to some extent to mimic the effects of sugar—triggering insulin secretion, inflammation and changes to the [gut microbiome](#)—which promote fat storage and type 2 diabetes," Hanover adds.

Since sweeteners are known to be passed on in small amounts via the placenta and breast milk, the researchers asked whether similar metabolic and microbiome changes occur in offspring following maternal sweetener intake. They fed mouse moms one of three sweetener solutions throughout pregnancy and lactation, and analyzed the effects on their pre-weaned pups. The solutions contained a mixture

of sucralose and acesulfame-K at the 'acceptable daily intake' (ADI), double the ADI, or a control (water). The ADI is the maximum consumption deemed safe in humans based on toxicology studies.

"Sweeteners are often used in combination, partly because a blend can reduce the unpleasant bitter taste that some consumers experience," explains Rother. Olivier Van-Stichelen adds, "Combining sweeteners might also amplify the metabolic and microbiome effects—so we used the typical pairing of sucralose and ace-K to maximize the applicability of our results."

Maternal sweetener consumption affects pre-weaned offspring

Analysis of blood, feces and urine from a total of 226 pups confirmed that both sweeteners are transmitted prenatally—and as predicted, affect the metabolism and microbiome of the offspring.

While the pups' exposure was low, the researchers found significant metabolic changes in both the ADI and 2xADI groups versus the control group. Specifically, these changes indicated impaired liver functioning in clearing toxins from the blood, and a dramatic shift in bacterial metabolites in the gut. In both sweetener groups, for example, the researchers observed the loss of a major beneficial species of gut bacteria, *Akkermansia muciniphila*. Similar microbiome alterations in humans have been linked to type 2 diabetes and obesity.

Should pregnant or lactating mothers avoid sweeteners?

"Our results showed dose-dependent effects of sweetener exposure," the researchers report.

Of note, the degree of metabolic change was far greater in the 2xADI than the ADI group. What's more, further changes in sweetener-exposed pups—including lower weight and fasting blood glucose—only became prevalent in the 2xADI group. However, the microbiome changes were drastic even at the acceptable daily intake level.

Current recommendations for artificial [sweetener](#) use during pregnancy state that they may be used in moderation—except for saccharin, which should be avoided entirely. However, artificial sweeteners are now found in more products than ever—including mouthwash, toothpaste, and medicines, as well as food and drink—and since labels do not specify the amounts of added sweeteners, it is impossible to accurately track our intake.

"The results of the study highlight yet another potential health impact of zero-calorie sweeteners," says Olivier-Van Stichelen. "This is [ongoing research](#) that will be continued both in my recently started lab at the Medical College of Wisconsin as well as in Drs. Hanover's and Rother's labs at the National Institutes of Health".

Dr. Hanover concludes: "The perinatal period is a critical developmental stage for the microbiome and emerging detoxification systems in the rodent and human neonate alike, and our study defines potentially adverse consequences of early exposure to sweeteners. Therefore, based on our findings, zero-calorie sweeteners warrant further investigation in humans in this critical developmental window."

More information: Stephanie Olivier-Van Stichelen et al, Maternal Exposure to Non-nutritive Sweeteners Impacts Progeny's Metabolism and Microbiome, *Frontiers in Microbiology* (2019). [DOI: 10.3389/fmicb.2019.01360](#)

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