International Sweeteners Association

FACTSHEET

Gut microbiota

and Low/no Calorie Sweeteners

Human studies show that low/no calorie sweeteners do not adversely affect the gut microbiota or human health when consumed at approved levels. Day-to-day dietary variation, unrelated to sweeteners, is likely a much more important driver of changes in the gut microbiome.

The human gut microbiota is a complex ecosystem of trillions of microorganisms that play essential roles in digestion, metabolism, immune function, protection against pathogens, and overall health. Disruptions in its composition and diversity – commonly referred to as *dysbiosis* – have been associated with obesity and metabolic diseases. However, there is still no consensus of what defines a "healthy" gut microbiome.[1]

Diet is one of the most important factors shaping this ecosystem, although responses can vary widely from person to person, depending on individual characteristics such as genetics, age, and baseline microbiota composition, as well as exposures from the external environment.[1]

The terms 'gut microbiota' and 'gut microbiome' are often used interchangeably but there's a subtle difference: '**microbiota**' refers to the microbes in our gut, while '**microbiome**' goes a step further covering the microbes, their genes, and the environment they form together.

How do low/no calorie sweeteners affect the gut microbiota?

Human studies

Evidence from human randomised controlled trials (RCTs), the gold-standard study design to establish a causal relation, indicates that low/no calorie sweeteners do not have a consistent or clinically meaningful impact on the gut microbiota when consumed within Acceptable Daily Intake (ADI) levels.[2,3]

A 2014 study published in *Nature* raised concerns about a potential link between saccharin, gut microbiota alterations, and glucose intolerance.[4] However, these findings were mainly based on animal experiments and a small, uncontrolled pilot study in just seven individuals. A subsequent well-designed, double-blind, placebo-controlled RCT addressing these limitations has not confirmed these effects when saccharin was consumed at ADI levels.[5]

Overall, most human trials – six out of eight RCTs available to date – report no significant changes in gut microbiota composition or key metabolites such as short-chain fatty acids following consumption of commonly used sweeteners, including aspartame, saccharin, sucralose, and stevia, or products containing them. [5-12]

Longer-term and real-world evidence provides additional context. The largest and longest RCT to date in adults with overweight or obesity found that regular consumption of low/ no calorie sweetened foods and beverages over one year was associated with a more favourable gut microbiota, including increased abundance of bacteria linked to beneficial metabolite production, alongside improved weight-loss maintenance.[13]

Preclinical evidence

Studies suggesting potential adverse effects are mainly based on *in vitro* and animal research, often using unrealistically high doses of sweeteners or systems with limited relevance to human physiology.[14,15] For example, differences between the rodent and human gut microbiome limit the biological relevance of animal study findings.

What to keep in mind when evaluating research on low/no calorie sweeteners and gut microbiota

Differences in how each sweetener is processed in the body, study design, dietary control, doses tested, and analytical methods can all influence results. Importantly, low/no calorie sweeteners are not all the same. Their absorption, metabolism, and excretion vary, meaning their interactions with gut microbes may differ and findings cannot be generalised across all sweeteners.[16]

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