



# An Update on Non-nutritive Sweeteners



Artificial sweeteners, also called alternative, non-nutritive, and low- or no-calorie sweeteners, are a popular ingredient in many foods and beverages. They create a sweet taste by stimulating sweet-taste receptors in the mouth, which then send signals to the brain. Recent research shows that these sweet-taste receptors are also located in other parts of the body like the gastrointestinal tract, pancreas, brain, and fat tissue. This discovery suggests that non-nutritive sweeteners (NNSs) may have broader effects on metabolism, as seen in various lab, animal, and human studies.

## Gut Microbiome

The effects of NNSs on gut microbiota are still being explored, with studies showing mixed results. NNSs can alter gut microbial composition and metabolic activity, potentially reducing beneficial bacteria while increasing pathogenic strains, which may lead to inflammation, gut dysbiosis, and changes in glucose metabolism. These effects, including shifts in short-chain, fatty-acid production, bile acid levels, and gut hormone release, highlight their potential role in metabolic and inflammatory diseases. Various NNSs may each react differently in the gut, for example, sucralose can potentially alter gut microbiota composition but aspartame does not. Sugar alcohols may promote beneficial bacteria and bolster production of short-chain fatty acids. Further research is needed to better understand how and why different types and doses of NNSs affect the gut and hunger hormone signaling and how long their impact lasts.

## Metabolic Health

A review published in *Cureus* evaluated the impact of NNSs on human health to determine risks and benefits of consumption. The review found that there was a significant association between NNS intake and blood sugar (increased

fasting levels and A1c as well as impaired glucose tolerance), weight gain in the midsection, and higher alanine aminotransferase levels, which can signal liver impairment. There was also a positive correlation between intake and delayed stomach emptying and intestinal transit; this may lead to increased gastrointestinal distress.

## CVD

The relationship between NNSs and CVD risk is as yet unclear, with some studies showing direct associations with adverse outcomes, while others find no harm. Data from a cohort study suggest that NNS intake, including aspartame, acesulfame-K, and sucralose, is linked to increased risks of cerebrovascular events and coronary heart disease. These findings indicate that replacing added sugars with some NNS may not provide cardiovascular benefits. Emerging evidence from *Advances in Nutrition* suggests sucralose may interact with bitter receptors called TAS2Rs in the cardiovascular system, potentially influencing blood pressure and vascular health through inotropic and vasodilator effects. However, further clinical studies are needed to clarify its long-term impact on cardiometabolic health.

## Neurological Impacts

Aspartame remains the primary NNS linked to neurological symptoms such as headaches, migraines, seizures, anxiety, depression, and insomnia. Its components, phenylalanine and aspartate, can increase brain levels of certain compounds that disrupt neurochemical balance, affecting dopamine, norepinephrine, and serotonin regulation. Additionally, aspartame may act as a chemical stressor by raising cortisol levels and oxidative stress. This may contribute to neurobehavioral health decline and migraine pathophysiology via serotonin-related vascular changes.

**Conclusion:** The World Health Organization recommends sugar should comprise no more than 5% of total energy intake, which is significantly lower than the average American intake of about 13%. Enjoying something sweet is a natural and joyful part of eating, therefore, using non-nutritive sweeteners is an alternative way to have something sweet while controlling caloric intake. Currently, high quality, evidence-based research revealing the impact of low- or no-calorie sweeteners on health remains inconclusive, and hinders the support of higher NNS intakes. Balanced dietary patterns are always encouraged, including a variety of nutrient-dense whole foods providing sufficient macro and micro-nutrients. This approach is likely to ensure high dietary quality and minimize the impact of occasional sweetener use.