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WHAT ARE MONK FRUIT SWEETENERS?

onk fruit, also known as *lo han* guo or Swingle fruit, is a small round fruit native to southern China. Monk fruit sweeteners are nocalorie sweeteners that can be used to lower one's intake of added sugars, while still providing satisfaction to enjoy the taste of something sweet. Some types of sweeteners in this category are considered low-calorie — such as aspartame, and others are no-calorie (e.g., monk fruit sweeteners, stevia sweeteners and sucralose). However, collectively they are often referred to as sugar substitutes, high-intensity sweeteners, nonnutritive sweeteners, low- and no-calorie sweeteners or simply low-calorie sweeteners.

Like other no-calorie sweeteners, monk fruit sweeteners are intensely sweet. Monk fruit sweeteners range from being 150-200 times sweeter than sugar, and as such only small amounts are needed in a product to equal the sweetness provided by sugar. Monk fruit sweeteners can be used in a wide range of beverages and foods like soft drinks, juices, dairy products, desserts, candies and condiments. Because they are stable at high temperatures, monk fruit sweeteners can be used in baked goods. However, a recipe that uses monk fruit sweeteners in place of sugar may turn out slightly different because in addition to sweetness, sugar plays several roles in recipes related to volume and texture, but this varies based on the type of recipe.

Several brands, such as Monk Fruit In The Raw®, Lakanto®, SPLENDA® Monk Fruit Sweetener, SweetLeaf® and Whole Earth® use monk fruit sweeteners in granular and liquid forms.

HOW ARE MONK FRUIT SWEETENERS PRODUCED?

Monk Fruit has been used for centuries in Eastern medicine as both a cold and digestive aid. Extracts from monk fruit are also being used in tabletop sweeteners and to sweeten packaged foods and beverages.

Monk fruit sweeteners are produced by removing the seeds and skin of

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the fruit, crushing the fruit, and then filtering and extracting its sweet portions into liquid and powdered forms. During the production of monk fruit sweeteners, monk fruit extract is often blended with erythritol in order to taste and look more like table sugar. Erythritol is a type of polyol, also referred to as a sugar alcohol, that contains zero calories per gram.

WHAT HAPPENS TO MONK FRUIT SWEETENERS AFTER CONSUMPTION?

The compounds that give monk fruit extract its sweetness are called mogrosides, which consist of a backbone structure called mogrol with glucose units (glycosides) attached to it. The main mogroside in monk fruit sweeteners is mogroside V.

Most of what is known about how mogrosides are metabolized comes from studies done in animals. Animals are thought to metabolize mogrosides the same or similarly to humans. Mogrosides are not absorbed in the upper gastrointestinal tract, thus they do not provide calories. When mogrosides reach the colon, gut microbes cleave off the glucose molecules and use them as an energy source. The mogrol and some metabolites are then primarily excreted from the gastrointestinal tract, and minor amounts are absorbed into the bloodstream and excreted in the urine.2-4

Some monk fruit sweeteners contain erythritol. Erythritol is rapidly absorbed in the small intestine and the majority — 80-90% is excreted in the urine within 24 hours.^{5,6}



ARE MONK FRUIT SWEETENERS SAFE TO CONSUME?

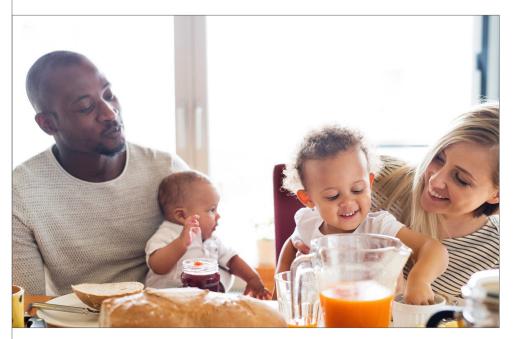
YES. Extracts from monk fruit are Generally Recognized As Safe (GRAS),⁷ a regulatory review process category used by the U.S. Food and Drug Administration (FDA). The FDA also lists erythritol as GRAS for use in a variety of foods and beverages.⁸ GRAS requires expert consensus that a food ingredient is safe for its intended use. In 2010, the FDA responded with no objections to the first GRAS notice submitted on extracts from monk fruit — whose scientific name is *Siraitia grosvenorii*. For more on the GRAS process, see the "What is GRAS?" sidebar.

The scientific opinion of the European Food Safety Authority (EFSA) published in 2019 stated that data was insufficient at that time for EFSA to make a conclusion on the safety of using monk fruit extracts in foods.⁹ The safety of monk fruit extract

has been confirmed by health agencies in countries around the world, including: China, Japan's Ministry of Health, Labour and Welfare, Food Standards Australia New Zealand (FSANZ) and Health Canada, which permit it in tabletop sweetener packets only. In its approval of the use of monk fruit extracts as a sweetener, FSANZ cites a history of safe use in China, Canada, Japan and the U.S., and no evidence of adverse effects in human studies from consuming up to 60 milligrams (mg) of monk fruit extract per kilogram (kg) of body weight per day.10 In animal studies, feeding extremely high levels of monk fruit extract (e.g., 2,500-7,000 mg of monk fruit extract per kg of body weight per day), adverse effects have not been clearly demonstrated. 11-13

Monk fruit extract is currently permitted for use in more than 60 countries, however an acceptable daily intake (ADI) has not been established. The ADI typically represents an amount 100 times less than the quantity of





a substance found to achieve a noobserved-adverse-effect-level in toxicology studies. According to the FDA, there are several reasons why an ADI might not be established for a substance, including evidence of safety at consumption levels that are well above the amount needed to sweeten a food or beverage.¹⁴ For more on ADI, see the "What is an ADI?" sidebar.

CAN CHILDREN CONSUME MONK FRUIT SWEETENERS?

YES. While no research has been published on monk fruit sweetener intake in children, no negative effects on health have been demonstrated in animal models or adults.¹⁰ Monk fruit sweeteners can add sweetness to a child's foods and beverages without contributing to calories consumed or added sugars intake. Monk fruit sweeteners are not fermentable like sugars and erythritol is noncariogenic.¹⁷ meaning it does not promote tooth decay.

With a focus on reducing consumption of added sugars in recent decades, the number of food

and beverage products containing low-calorie sweeteners has increased. Observational research among U.S. children and adults has shown an increase in the percentage of people reporting daily consumption of products containing low-calorie sweeteners; nevertheless, current intake of each low-calorie sweetener is considered to be well within acceptable levels, both globally and in the U.S. 19.20

The American Heart Association (AHA) advises against children regularly consuming beverages containing low-calorie sweeteners; instead the AHA recommends water and other unsweetened beverages such as plain milk.²¹One of the notable exceptions in the 2018 AHA science advisory is made for children with diabetes, whose blood glucose management may be benefitted by consuming lowcalorie-sweetened beverages in place of sugar-sweetened varieties. Citing an absence of data, the 2019 policy statement from the American Academy of Pediatrics (AAP) does not provide advice on children under two years of age consuming foods or beverages that contain low-calorie sweeteners.²²

WHAT IS AN ADI?

The acceptable daily intake, or ADI. is the average daily intake over a lifetime that is expected to be safe based on significant research.¹⁵ It is derived by determining the no-observed-adverse-effect-level, or NOAEL, which is the highest intake level found to have no adverse effects in lifetime studies in animal models, divided by 100.16 Setting the ADI 100 times lower than the upper level found to have no adverse effects in toxicology studies adds a margin of safety that helps to ensure that human intakes will be safe.

WHAT IS GRAS?

Food ingredients permitted for use in the U.S. fall into one of two categories: food additives, which require review prior to approval from the FDA; or Generally Recognized as Safe (GRAS) ingredients. Whether GRAS or a food additive, food ingredients must be safe and must meet the same high food safety standards. To be considered GRAS, an ingredient must meet one of the following two conditions:

- 1) A history of safe use has been established and a significant number of people consumed the ingredient prior to the enactment of the Food Drug and Cosmetic Act of 1958; or
- 2) Scientific data and information about the safety and use of the ingredient are widely known and publicly available in scientific articles, position papers, and the like, with consensus among scientific experts that the ingredient is safe for its intended use.



The 2019 AAP policy statement does, however, acknowledge the potential benefits of low-calorie sweeteners for children: those benefits include reducing calorie intake (especially among children with obesity), incidence of dental caries and glycemic response among children with Type 1 and Type 2 diabetes. The 2020-2025 Dietary Guidelines for Americans (DGA) do not recommend the consumption of low-calorie sweeteners or added sugars by children younger than two years of age.23 This DGA recommendation is not related to body weight, diabetes or the safety of added sugars or low-calorie sweeteners; instead it is intended to avoid infants and toddlers developing a preference for overly sweet foods during this formative phase.

CAN PREGNANT AND BREASTFEEDING WOMEN CONSUME MONK FRUIT SWEETENERS?

YES. Although no published research has examined possible effects of monk fruit sweeteners on pregnant and lactating women, several studies in animals have demonstrated no adverse reproductive or developmental effects to a mother or offspring, even when animals were exposed to very high levels of monk fruit sweeteners every day over long periods of time.¹⁰ All women who are pregnant or



nursing need the necessary nutrients and calories for their baby's optimal growth and development, while taking care not to exceed their needs.

CAN PEOPLE WITH DIABETES CONSUME MONK FRUIT SWEETENERS?

YES. Foods and beverages made with low- and no-calorie sweeteners such as monk fruit sweeteners are frequently recommended to people with diabetes as an alternative to sugar-sweetened foods and beverages; they are also recommended as a way to help these individuals satisfy their desire for sweet taste while managing carbohydrate intake.

The impact of monk fruit sweetener consumption has not been studied in individuals with Type 2 diabetes. Some observational studies have demonstrated an association between low-calorie sweetener consumption and risk for Type 2 diabetes;^{24,25} however, because none of the studies included monk fruit sweeteners, no evidence of an association between the reported consumption of monk fruit sweeteners and Type 2 diabetes has been described in the published literature.

A 2017 randomized controlled trial tested the glycemic response of people without Type 2 diabetes after consuming monk fruit sweeteners.^{26,27} In this small cross-over study of young men, post-prandial blood glucose^{26,27} and insulin levels²⁶ did not differ between pre-meal consumption of beverages containing monk fruit sweeteners, stevia sweeteners or aspartame. Unpublished reports that were cited by the EFSA in their 2019 Scientific Opinion demonstrated that human consumption of a single dose of 200 mg/kg of body weight per day of monk fruit sweeteners had no effect on blood glucose,9 although the monk fruit extract





concentrations were not reported.

Recent consensus statements by experts in nutrition, medicine, physical activity and public health, have concluded that the use of lowcalorie sweeteners may contribute to better glycemic management among people with diabetes due to the neutral effects of low-calorie sweeteners on hemoglobin A1c, insulin, and fasting and post-prandial glucose.²⁸⁻³⁰ Global health professional organizations have also published conclusions on the safety and role of low-calorie sweeteners for people with diabetes. The 2021 American Diabetes Association Standards of Medical Care in Diabetes states that "For some people with diabetes who are accustomed to regularly consuming sugar-sweetened products, nonnutritive sweeteners (containing few or no calories) may be an acceptable substitute for nutritive sweeteners (those containing calories, such as sugar, honey, and agave syrup) when consumed in moderation. Use of nonnutritive sweeteners does not appear to have a significant effect on glycemic management,

but they can reduce overall calorie and carbohydrate intake, as long as individuals are not compensating with additional calories from other food sources."³¹ Similar statements addressing the safety and potential use of low-calorie sweeteners for people with diabetes are supported by <u>Diabetes Canada</u>³² and <u>Diabetes UK</u>.³³

CAN MONK FRUIT SWEETENERS HELP WITH WEIGHT LOSS OR WEIGHT MAINTENANCE?

At present, no research in humans, either observational or interventional, has directly examined how the consumption of monk fruit sweeteners is associated with, or affects body weight. Most of the scientific research examining the relationship between low-calorie sweetener intake and body weight collectively assesses consumption of foods and beverages that contain multiple types of low-calorie sweeteners, including sweetener blends. One example is an online survey of 434 members of The National Weight Control Registry (NWCR); it

is the largest longitudinal study of successful weight loss maintainers who have lost at least 30 pounds and kept if off for more than one year.³⁴ The NWCR survey found that more than 50% reported that they regularly consumed low-calorie-sweetened beverages; 78% of these individuals reported that doing so helped control their calorie intake.

Some observational studies have reported an association between the use of low-calorie sweeteners and increased body weight and waist circumference in adults.35 A systematic review and meta-analysis of observational studies published in 2017 found that consumption of low-calorie sweeteners was also associated with increases in body mass index (BMI) and higher incidence of obesity and cardiometabolic disease in adults.³⁶ Other recent systematic reviews and meta-analyses have concluded that findings from observational studies showed no association between lowcalorie sweetener intake and body weight, and a small positive association with higher BMI.³⁷⁻³⁹ In children and adolescents, observational studies have shown an association between consumption of low-calorie-sweetened beverages and increased body weight, although evidence from randomized controlled trials have not.40,41

Observational studies can be important for generating hypotheses, but it is important to note that they have limitations. By their nature, observational studies cannot prove cause and effect. Instead, observational studies examine the association between an exposure — such as reported intake of low-calorie sweeteners, and an outcome, such as body weight or a health condition. Associations found in observational studies can be confounded by various factors and/or may be the result of reverse causality. A common example





of this is a person changing their food and beverage choices after being diagnosed with a health condition; the disease led to them making these changes but the changes they made did not lead to the disease.

It has also been suggested that people who already have overweight or obesity may begin to choose low-calorie-sweetened foods and beverages as one method for losing weight.42-45 This makes it difficult to assume that the use of a low-calorie sweetener can be the cause of weight gain, since reverse causality may be a factor. A 2019 systematic review and meta-analysis funded by the World Health Organization recommended to cautiously interpret results from observational studies on low-calorie sweeteners and health outcomes. while concentrating on plausible confounding and reverse causality.³⁹

Another difficulty in studying the impact of low-calorie sweeteners on body weight is that people may compensate for calorie-free choices by eating or drinking more calories in other food choices or future meals.46,47 Think of a person who may justify ordering dessert at a restaurant because he or she had a diet soda with their meal: the extra calories from the dessert will likely be greater than the calories saved by ordering the diet beverage. These additional calories may contribute to weight gain or prevent further weight loss. This behavior is called the "licensing effect" or "self-licensing." in which an individual rationalizes indulgences by finding reasons to make a behavior that is inconsistent with their goals more acceptable.⁴⁸ Although it may occur in some instances, there is little evidence from scientific studies that people consistently and consciously overconsume calories as a result of consuming low-calorie sweeteners, or foods and



MONK FRUIT SWEETENERS AT A GLANCE

SCIENTIFIC NAME: Siraitia grosvenorii

BRAND NAME: Monk Fruit In The Raw®, Lakanto®, SPLENDA® Monk Fruit Sweetener, SweetLeaf®. Whole Earth®

FDA STATUS: Generally Recognized As Safe (GRAS) in 2010 for use in foods and beverages

beverages that contain them.⁴⁹

Well-designed randomized controlled trials are considered to be the gold standard for assessing causal effects. Evidence from randomized controlled trials support that substituting low-calorie sweetener options for regular-calorie versions leads to modest weight loss. 37-39,50-53 In a 2016 randomized clinical trial, over 300 participants were assigned to consume either water or low-caloriesweetened beverages for one year as part of a program that included 12 weeks of weight loss followed by 40 weeks of weight maintenance interventions. Those who were assigned to the low-calorie-sweetened beverage group lost 6.21 kg on average; those in the water group lost 2.45 kg.⁵⁰

Conclusions from observational research studying the impact of low-calorie sweeteners on body weight often conflict with data from randomized controlled trials.

A 2018 review of the relevant scientific literature concluded that evidence from observational studies show an association between lowcalorie sweetener intake and higher body weight; however, evidence from randomized controlled trials demonstrate that low-calorie sweetener consumption may support weight loss.54 More recently, a 2021 citation network analysis found that literature reviews that show a relationship between low-calorie sweetener intake and lower body weight mostly rely on data from randomized controlled trials, whereas reviews that cite mostly observational studies show a relationship with higher body weight.55

While a few systematic reviews of intervention trials have concluded that low-calorie sweetener consumption does not lead to appreciable weight loss or weight gain, such findings appear to be the result of how the studies are compared.³⁶ As stated



by Mela, et al.,⁴⁵ some study designs allow for the analysis of outcomes between caloric and non-caloric alternatives,^{38,53} while others do not.³⁶

The Scientific Report of the 2020 Dietary Guidelines Advisory Committee (DGAC) included a systematic review of 37 studies — six of which were randomized controlled trials, published between January 2000 and June 2019, on the role of low-calorie-sweetened beverages on adiposity. The DGAC report concluded that low- and no-calorie sweeteners should be considered an option for managing body weight.⁵⁶

It is important to note that losing and maintaining body weight requires multiple simultaneous approaches. Making a single change, such as substituting low-calorie sweeteners for full-calorie, sugar-containing products, is just one component. Lifestyle and behavioral practices like eating healthfully, exercising regularly, getting enough sleep, and maintaining social support networks are all important factors in achieving weight loss and weight-maintenance goals.

CAN MONK FRUIT SWEETENERS MAKE ME HUNGRIER?

Highly palatable foods activate brain regions of reward and pleasure. This positive association has been hypothesized to enhance appetite, and if left unchecked, the resulting increase in food intake may contribute to overweight and obesity.⁵⁷ Low-calorie sweeteners can also lead to a stimulation of reward pathways by activating sweet taste receptors, but they are not a source of calories.

Some have expressed concern that activating reward pathways without delivering calories to the body may have unintended consequences but



more research is needed to support this hypothesis. Some animal studies have demonstrated changes in food intake and appetite-related hormones after consuming low-calorie sweeteners. However, other animal studies show that pathways involved in sugar digestion and preference for sugar are not activated by low-calorie sweeteners. 58,59

Although little research has been published on the specific effects of monk fruit sweetener intake on human appetite and satiety, other low- and nocalorie sweeteners have been studied more extensively. To date, there is no strong evidence that low- and nocalorie sweeteners enhance appetite or cravings in humans. South Some randomized controlled trials have demonstrated the opposite effect, including a decrease in hunger and reduced dessert intake compared

with those who drank water.⁶⁴ A small 2017 randomized controlled trial was the first to investigate the effects of a monk fruit-sweetened beverage on subsequent calorie intake. Results from the study of 30 young men showed that calorie intake did not differ during a 24-hour period when either a pre-lunch beverage sweetened with monk fruit sweeteners, or a sucrose-sweetened beverage was consumed.²⁶

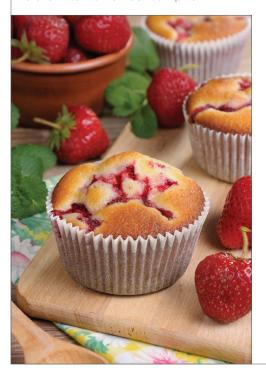
WHAT ABOUT THE MICROBIOME?

Although research on the gut microbiome is still in its infancy, the microbes living in the intestinal tract have become recognized as potentially significant contributors to health. However, no standards currently exist to define a healthy human microbiome.⁶⁵ There are significant



differences among the microbiome profiles of different people, and research has shown that the gut microbiome can quickly respond to normal changes in food choices. ⁶⁶ International experts have noted that huge variabilities in microbiome profiles makes it difficult to distinguish normal variation from adverse effects.

Despite the involvement of the gut microbiota in the metabolism of monk fruit's mogrosides, to date there is no evidence that monk fruit sweeteners meaningfully impact the composition or function of the gut microbiome. However, randomized clinical trials have not yet been conducted in humans. A 2019 literature review found no conclusive evidence that lowcalorie sweeteners negatively impact gut microbiota.⁶⁷ In 2020, a panel of experts on low-calorie sweeteners came to a similar conclusion that, at this time, data on the effects of lowcalorie sweeteners on the human gut microbiota are limited and do not provide adequate evidence that they impact out health at doses that are relevant to human consumption.^{30,68}





WHAT IS THE BOTTOM LINE?

All types of foods and beverages, including those made with monk fruit sweeteners, can have a place in a variety of healthy eating patterns. Monk fruit sweeteners are relatively new to the food supply. As such, their impact on, and association with, chronic conditions like obesity and diabetes have not been well studied as it has been for other lowcalorie sweeteners. However, monk fruit sweeteners have been safely used for centuries in Asian cultures and no adverse effects have been documented. Monk fruit sweeteners have been considered GRAS in the United States since 2010 and their safety has been acknowledged by many international health agencies.

Monk fruit sweeteners have not been directly studied for their impact on body weight as they have on other low-calorie sweeteners. Results from observational studies on the impact of low-calorie sweeteners on body weight often conflict with results from randomized controlled trials. Observational studies linking low-calorie sweeteners to weight gain or risk for diabetes inherently cannot

demonstrate a causal relationship and suffer from methodological issues like confounding and reverse causality. In contrast, randomized controlled trials consistently support that the use of low-calorie sweeteners can be a useful nutrition strategy to assist with weightloss and/or weight-maintenance goals. Randomized controlled trials also support that low-calorie sweeteners do not impact blood glucose or insulin levels, including the only published randomized controlled trial conducted on glycemic and insulinemic effects of consuming monk fruit sweeteners. While the role of the gut microbiome in health is still being explored, the available research does not suggest that low- and no-calorie sweeteners adversely affect the gut microbiome.

Adopting a healthful, active lifestyle that is tailored to personal goals and priorities is vital to supporting one's well-being. Choosing foods and beverages sweetened with lowand no-calorie sweeteners such as monk fruit sweeteners is one way to reduce consumption of added sugars and manage calorie intake, which are important components in maintaining health and reducing risk for lifestyle-related disease.



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