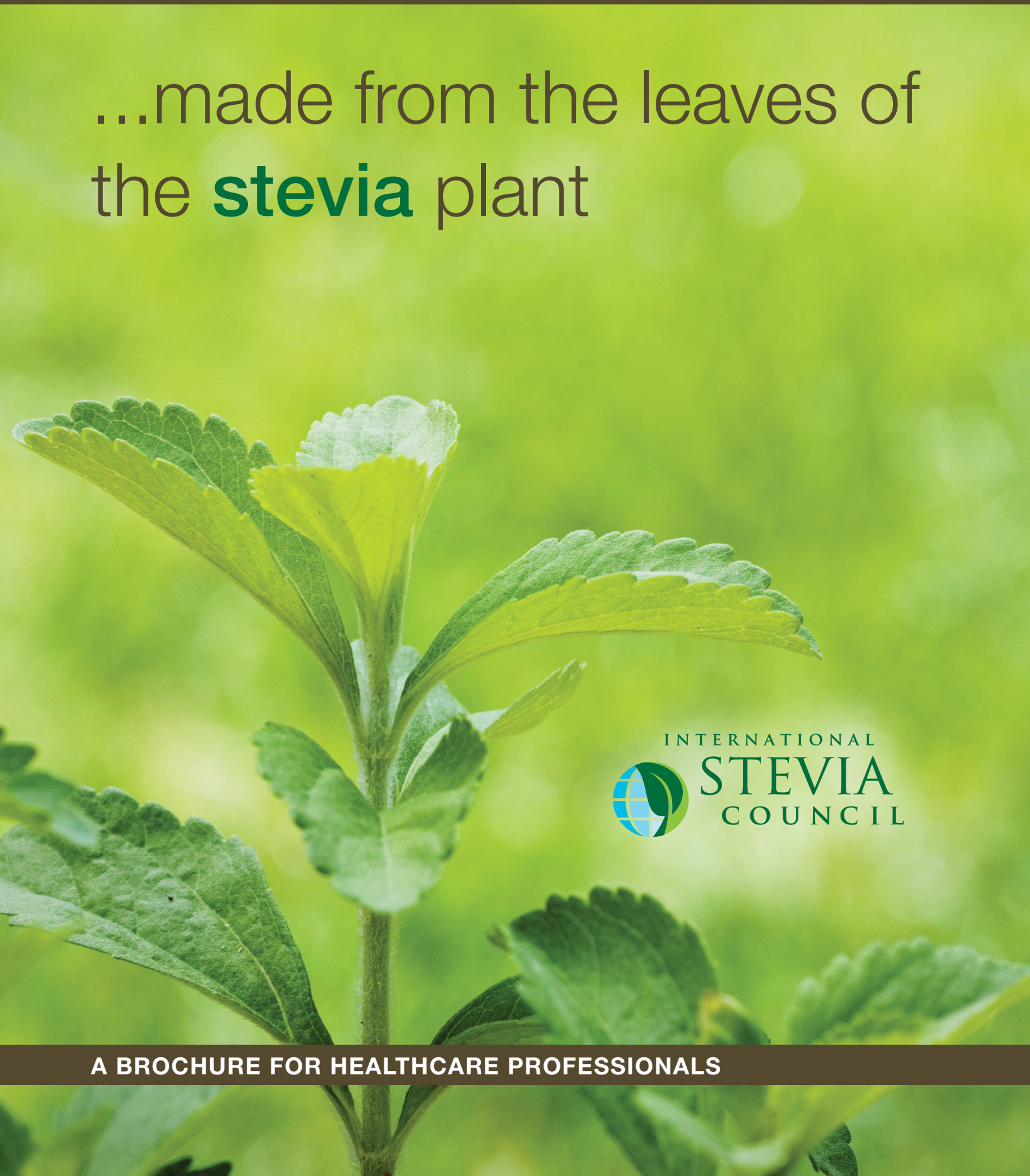
The new sweetener from natural origins...

...made from the leaves of the **stevia** plant



INTERNATIONAL STEVIA COUNCIL

A BROCHURE FOR HEALTHCARE PROFESSIONALS

Contents

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Introduction

Stevia leaf extracts are calorie-free sweeteners of natural origin, derived from the stevia plant, a shrub native to South America. The sweet components of the stevia plant, steviol glycosides, are naturally found in the plant's leaves and are between 200 and 300 times sweeter than sucrose, calorie-free, and do not have an effect on the Glycemic Index. Therefore, stevia leaf extracts offer an innovative solution to assist people in weight management and in budgeting total caloric intake.

Stevia leaf extracts can improve the diet and health of people globally by reducing sugar and calorie intake in food.

This brochure aims to provide healthcare professionals with information on stevia leaf extracts and steviol glycosides, along with their benefits, safety and a body of evidence that supports the approval of stevia leaf extracts as sweeteners worldwide.

Nutritional benefits of stevia leaf extracts

Overweight populations and obesity rates continue to rise in many parts of the world. This has had a direct impact on the prevalence of chronic diseases such as type 2 diabetes and metabolic syndrome. While it is important to promote and encourage improvements in dietary habits and physical activity levels, it is also critical to equip patients with the right tools to support long term changes. It is widely recognized that humans have a preference for sweet tasting foods. As such, the use of low calorie sweetener substitutes, like stevia leaf extracts, can be applied to support the long term adherence to a healthful diet by reducing caloric intake throughout the day.

Reduction of calories

There seems to be confusion as to whether stevia leaf extracts (and steviol glycosides) are zero calorie. Steviol glycoside molecules contain linked sugars (primarily glucose), but are resistant to digestion by the human body. As such, they do not break down in the body until they reach bacteria in the colon, where sugars are cleaved from the molecule. The remaining steviol unit

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is converted to steviol glucuronide and is excreted in the urine stream. However, stevia leaf sweeteners are consumed daily in such low amounts (on average, they are 200–300 times sweeter than sucrose) that colonic metabolism of the sugar molecules does not significantly contribute to daily caloric intake. Replacing nutritive sweeteners in part or whole with stevia leaf extract sweeteners on a sugar equivalent basis, allows for significant calorie reduction. However, it's also important to account for caloric contribution of other ingredients in the formulation.

From the plant to a sweetener of natural origin

The stevia plant is native to South America and has been used for centuries as a sweet herb, called "Kaà he'e" by indigenous populations. Traditionally, the plant leaves were dried and used to sweeten maté, teas and medicines, or simply chewed. The plant was first scientifically recorded in 1901 as Eupatorium rebaudianum by Moises Santiago de Bertoni, in Paraguay. In 1905, it was later classified as *Stevia rebaudiana* Bertoni, a member of the sunflower (Compositae) family.[1]

The sweetness of the stevia plant is attributed to the existence of sweet constituents in the leaves of the plant. These constituents, also known as steviol glycosides, were first identified individually by French researchers, M. Bridel and R. Lavielle, in 1931 for their sweetening power — between 200 and 300 times as sweet as sucrose.

Stevia is now grown in home gardens and commercially cultivated in Paraguay, Kenya, China and the United States, and in many other parts of the world, including Vietnam, Brazil, India and Colombia.

Stevia and its leaf extracts have been used for centuries, but today's stevia leaf extracts can be produced at high purity levels for food and beverage use. Steviol glycoside purification occurs in several stages, as they are isolated from the stevia leaves using traditional extraction methods. The extraction process involves steeping the dried leaves of the stevia plant in water, then filtering and separating the liquid from the leaves and stems. In the second stage, the cleared solution of stevia extract is further purified with either water and/or food grade alcohol — all conventional plant extraction methods — and is concentrated to meet regulatory specifications. The purified stevia extract may then pass through multiple crystallization steps to enhance the purity of one or more specific steviol glycosides.[2,3]

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There are at least 10 known steviol glycosides in the stevia leaf with stevioside and rebaudioside A being the most prevalent.

Stevia leaf extracts were first commercially adopted as sweeteners in Japan in the 1970s, where they remain a popular ingredient.[1,4] In recent years, the demand for sweetness from a natural source has supported stevia leaf extracts' development for the global marketplace. Combined with consumer demand for low-calorie sweetness, and global acceptance as a safe and effective sweetener, stevia leaf extracts are well-suited to become the world's next mainstream sweetener. These extracts offer consumers a unique option as a sweetener — natural like sugar, but without the calories.

Stevia leaf extracts deliver a number of tangible benefits to food producers and their customers. The proven stability of steviol glycosides at different pH levels and temperatures contribute to their shelf-life and functional robustness across food processing conditions, including cooking, baking, freezing, HTST and UHT processes, making stevia leaf extracts suitable for use in a wide range of food and beverage products.[5]

Clinical and experimental data on the safety of steviol glycosides

The safety of steviol glycosides has been extensively reviewed in published literature and by national and international food safety authorities. The Joint FAO/WHO Expert Committee on Food Additives (JECFA), the European Food Safety Authority (EFSA) and GRAS (Generally Recognized As Safe) independent expert panels in the United States, concluded that steviol glycosides, extracted from stevia, are not genotoxic or carcinogenic.

Extensive experimental data are available for steviol glycosides. These data come from *in vitro* and *in vivo* experiments with animals, as well as comprehensive human studies. The main conclusions for human health are as follows:

- Studies on steviol glycoside metabolism show that after oral administration, steviol glycosides are poorly absorbed by the upper intestinal tract[6-8] and are metabolized by intestinal microflora in the lower intestinal tract to steviol,[9-11] which itself is absorbed from the intestinal tract. The absorbed steviol is rapidly conjugated with glucuronic acid and then eliminated from the body via urine excretion. The reaction is called glucuronidation. The human body uses glucuronidation to make a large variety of substances more water-soluble, and in this way, allow for their subsequent elimination from the body. This reaction is very common in humans and other species to facilitate the removal of substances from the body. Many other substances we ingest go through this same pathway. Pharmacokinetic results indicate that steviol glycosides undergo an elimination pathway with steviol glucuronide excreted primarily the urine.

Results of toxicological studies show that steviol glycosides have no genotoxic or carcinogenic effects and are not toxic to the reproductive system of animals, even in high doses over an entire lifetime:

- Concerning the potential for effects on glucose homeostasis, in doses consistent with, and exceeding, the acceptable daily intake, no increase in glycemia, HbA1c or plasma insulin has been observed among healthy subjects, nor among subjects with type 2 diabetes.[12,13]
- Steviol glycosides are non-cariogenic. They do not lower dental plaque pH and are therefore tooth friendly.[14,15]

> ...global experts...concluded that steviol glycosides, extracted from stevia, are not genotoxic or carcinogenic.

To summarize: On the basis of the studies conducted, global experts, including: the Joint FAO/WHO Expert Committee on Food Additives (JECFA), European Food Safety Authority (EFSA) and GRAS (Generally Recognized As Safe) independent expert panels in the United States, concluded that steviol glycosides, extracted from stevia, are not genotoxic or carcinogenic. These experts have also concluded that steviol glycosides do not pose risk during the human reproduction cycle or development life stages.

A review of additional genotoxicity studies published since 2008 found one new set of genotoxicity studies (*in vitro* and *in vivo* assays) on rebaudioside A.[16] No genotoxic effects were found in any of the assays.

Stevia leaf extract sweeteners: regulatory authorizations and approvals

A timeline of international safety and health evaluations

The safety of steviol glycosides extracted from leaves of the stevia plant has been established based on three elements: the use of stevia leaf extracts worldwide, scientific research and positive safety opinions.

Stevia leaf extracts long history of use around the world

A long time before Moises Bertoni heard of Kaà he'e (the historical native name of the Stevia rebaudiana plant) in Paraguay at the end of the 19th century, the leaves where used by the native Guaraní to reduce the bitter astringent taste of maté tea and to sweeten food. The plant was a wild growing species in East Paraguay.[17,18]

More than 25 years of scientific research on the sweet-tasting substances in the stevia leaf (steviol glycosides)

Numerous studies have been conducted to show the safety of steviol glycosides. Today's knowledge about the sweeteners' metabolism and toxikokinetics, acute, chronic and sub-chronic toxicity, genotoxicity, carcinogenicity, reproduction and developmental toxicity as well as other effects on the body is well established and advanced, and leads to the approval of its use as an intense sweetener in food in most regions of the world.[19-22]

Positive safety opinions by leading regulatory authorities

Positive safety opinions and responses from global food safety authorities, including the World Health Organization/Joint Expert Committee on Food Additives, the European Food Safety Authority, and the US Food and Drug Administration, are opening worldwide markets for this new sweetener.

Prior to 2008

Stevia leaf extracts were authorized for use in a variety of countries in South America and Asia before 2008. Japan is the leading and pioneering country when it comes to the use of steviol glycosides as high intensity sweeteners in food and beverages. The first commercial stevia leaf extracts were established in Japan in the early 1970s. So far, there are no safety concerns noted during this 40 years of use.

2008

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) determined that steviol glycosides are safe for use as a food and beverage sweetener. JECFA established a permanent Acceptable Daily Intake (ADI) of 0–4 mg/kg body weight (expressed as steviol equivalents) which was established at the 69th JECFA in 2008 and published in FAO JECFA Monographs 5.[23]

The US Food and Drug Administration (FDA) concluded in December 2008 that it had no objection to rebaudioside A at 95 percent purity or above, having GRAS (Generally Recognized As Safe) status as a general purpose sweetener for use in food and drink, not just as a supplement. This was concluded after two separate applicants notified the FDA that the new natural, zero calorie sweetener met FDA GRAS status through independent expert panels, and submitted evidence to show that it is safe for use in the food supply.[24]

Australia and New Zealand Food Safety Authority (FSANZ) approved purified stevia sweeteners for use in a variety of foods and beverages.[25]

2009

The use of rebaudioside A is authorized in France, after the French Food Safety Agency considered that the use of rebaudioside A extracted from the stevia plant, with a purity level of at least 97%, does not present a health risk for consumers.[26,27]

2010

The European Food Safety Authority (EFSA) assessed the safety of steviol glycosides and established an Acceptable Daily Intake (ADI) for their safe use. After considering all data on stability, degradation products, metabolism and toxicology, the panel set an ADI of 4 mg/kg body weight per day for steviol glycosides (expressed as steviol equivalents), a level consistent with that established by JECFA.[28]

2011

The Codex Alimentarius adopted a variety of food and beverage uses for steviol glycosides into the Global Standard for Food Additives (GSFA).[29] The European Union authorized steviol glycosides (E 960), the first high intensity sweetener of natural origin, for use in a variety of food and beverages.[30]

2012

Canada – Health Canada approved the use of steviol glycosides as a table-top sweetener and as a sweetener in certain food categories.[31]

South Africa – Stevia was finally approved for use in South Africa with the recent promulgation (10 September 2012) of new sweetener regulations.[32]

Indonesia – Indonesia approved steviol glycosides as natural sweeteners in 2012.[33]

2013

The approval of steviol glycosides was granted in Thailand in 2013 and is anticipated to be finalized in India.

Glossary of terms

What is the International Stevia Council (ISC)?

The ISC is a global trade association composed of companies that process, manufacture and/or market stevia leaf extract sweetener products. Our aim is to promote the use of naturally-sourced stevia leaf extract sweetener products that can improve the diets and health of people globally by addressing sugars and calories in foods and beverages.

Ingredient terminology

Stevia (*Stevia rebaudiana* Bertoni) – Stevia is a perennial plant from the Sunflower family, with the benefit of sweet-tasting leaves. The plant was first classified in 1905 by Swiss scientist Moises Santiago Bertoni who named it *Stevia rebaudiana* Bertoni.

Steviol glycosides – Steviol glycosides is the collective name of the sweet components present in the stevia leaf. These sweet components consist of glucose molecules and in some instances, rhamnose and xylose molecules attached to the aglycone steviol (diterpene type). The two main components are stevioside and rebaudioside A. In addition, there are other associated glycosides present, such as rebaudioside B, C, D, F, dulcoside A, rubusoside, steviolbioside etc.

Rebaudioside A – Rebaudioside A is one of two major components present in the stevia leaf and it is best known for its clean, sweet taste. Its sweetness intensity is around 200 times that of sugar, but will vary depending on the food or beverage in which it is used.

Steviol equivalents – The adoption of the term Steviol Equivalents is part of the process of adopting a common method of measurement of steviol glycoside content. Steviol is a molecule that is common to the molecular structure of all steviol glycosides. As the molecular weights of the various steviol glycosides are different, JECFA has suggested that the concentrations/amounts of steviol glycosides should be expressed as steviol content. To obtain the steviol equivalents of the different steviol glycosides, their amounts should be multiplied by a given factor depending on whether it is rebaudioside A, rebaudioside C, etc.

Regulatory terminology

EFSA – The European Food Safety Authority (EFSA) has the responsibility for providing evaluations and scientific opinions in support of EU legislation on food.

FDA – The Food and Drug Administration (FDA or USFDA) is an agency of the United States Department of Health and Human Services, one of the United States federal executive departments. The FDA is responsible for protecting and promoting public health through the regulation and supervision of food safety, dietary supplements, etc.

Codex – Codex Alimentarius is a common program created by FAO and WHO in 1963 covering all foods and materials for foods. It develops food standards and guidelines and its objective is to protect consumers' health and to promote coordination of all food standards work undertaken by international governmental and non-governmental organizations.

GRAS – Generally Recognized as Safe (GRAS) is a regulatory designation used in the United States where substances added to food must either be approved by the Food and Drug Administration (FDA) as Food Additives, or are demonstrated through a self-affirmation process, to be generally recognized as safe (GRAS). Regardless of classification as a Food Additive or GRAS substance, both are required to meet the same level of safety requirements. There is no premarket notification required for GRAS substances, and the United States FDA offers a voluntary GRAS notification program whereby expert panel safety reviews of substances may be submitted to the FDA.

ADI – Acceptable Daily Intake (ADI) describes the amount of a food additive relative to body weight, which a person can consume without risk on a daily basis over a lifetime.

EDI – The Estimated Daily Intake (EDI) is a calculated estimate to determine the amount of a particular substance consumers could ingest per day. It is determined based on the concentration of that substance in a food, and the consumer intake of foods that might or will contain the substance.

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