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Review

Critical review of the current literature on the safety of sucralose

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ABSTRACT

Sucralose is a non-caloric high intensity sweetener that is approved globally for use in foods and beverages. This review provides an updated summary of the literature addressing the safety of use of sucralose. Studies reviewed include chemical characterization and stability, toxicokinetics in animals and humans, assessment of genotoxicity, and animal and human feeding studies. Endpoints evaluated include effects on growth, development, reproduction, neurotoxicity, immunotoxicity, carcinogenicity and overall health status. Human clinical studies investigated potential effects of repeated consumption in individuals with diabetes. Recent studies on the safety of sucralose focused on carcinogenic potential and the effect of sucralose on the gut microflora are reviewed. Following the discovery of sweet taste receptors in the gut and studies investigating the activation of these receptors by sucralose lead to numerous human clinical studies assessing the effect of sucralose on overall glycemic control. Estimated daily intakes of sucralose in different population subgroups, including recent studies on children with special dietary needs, consistently find that the intakes of sucralose in all members of the population remain well below the acceptable daily intake. Collectively, critical review of the extensive database of research demonstrates that sucralose is safe for its intended use as a non-caloric sugar alternative.

Contents

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Sucralose is a non-caloric sweetener that is widely approved globally for use in foods and beverages. It is derived from sucrose by the selective replacement of three hydroxyl groups by chlorine atoms. Sucralose has a sweetness potency of about 600 times that of sucrose, thus the addition of very small amounts of sucralose can be used to sweeten foods and beverages. Unlike sucrose, sucralose is not digested or metabolized for energy, therefore, no calories are obtained from sucralose, and sucralose does not affect blood glucose levels. These properties result in the use of sucralose to produce foods and beverages that are suitable for persons with diabetes or those aiming to reduce calorie or carbohydrate intake. Although several reviews have been published previously (Grice and Goldsmith, 2000: Grotz and Munro, 2009; JECFA, 1989a, 1991a; SCF, 1989, 2000a), the purposes of this review are (1) to provide an updated summary of the research investigating the safety of sucralose in one publication including studies that have been the genesis of new questions on sucralose safety, and (2) to provide background on the regulatory process of testing and approval of food additives for health professionals. Numerous clinical investigations into the effect of sucralose on glycemic responses are a particular focus, following the discovery of gut sweet taste receptors and academic studies investigating the potential role that activation of these has on overall glycemic control. Also reviewed are several recent studies that report on estimated daily sucralose intakes in different population subgroups, including children. Collectively, the data continue to demonstrate that sucralose is safe for its intended use as a non-caloric sugar alternative.

1. Background

1.1. History, regulatory status and health agency positions

The discovery and development of sucralose was the result of a collaborative research project of the Tate & Lyle Company and the Queen Elizabeth College of the University of London during the late 1980s (Knight, 1994). Extensive chemical characterization and toxicology studies were undertaken as required for premarket regulatory investigation into the safety of a proposed new food additive.

The general principles for the premarket safety assessment of new food additives, such as a non-caloric sweetener were first established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1958. Although these principles remain to be the basis for approvals by regulatory agencies globally, recent revisions incorporate current knowledge and advances in toxicological science (reviewed Magnuson et al., 2013). A detailed description of the studies required is publically available (WHO, 2009) and is similar to those required by other regulatory agencies including the Redbook by the US Food and Drug Administration (FDA), and the Organisation for Economic Co-operation and Development (OECD) (OECD, 1998; US FDA, 2000). These guidelines establish both the types of studies to be conducted and the appropriate study protocols to be used in investigating the safety of a new food ingredient. Regulatory agencies require complete chemical characterization of the ingredient, studies that demonstrate its intended functionality and stability in food, the method of manufacture, the detection method including data that validate the analytical method development, and comprehensive toxicological research. Toxicology testing requirements include evaluation of genetic effects, pharmacokinetics and metabolism, toxicology studies in rodents and in non-rodent species including life-time exposures to ensure no evidence of adverse effects on growth and development, organ function or structure, blood chemistry, and/or potential to cause cancer. Multigenerational studies assess possible effects on male or female reproduction, pregnancy, and offspring health and development. In addition, clinical studies are often conducted to compare the pharmacokinetics (absorption, distribution, metabolism and excretion) determined in experimental animals to data from humans, to demonstrate the appropriateness of the animal models used in safety testing. All data from the investigative studies must be submitted to the regulatory agencies. In the U.S., research studies submitted to FDA are available through a Freedom of Information Act request, and JECFA evaluations of the submitted toxicology studies, which form the basis for approvals in the EU and numerous other countries, are published and publicly available online. Manufacturers of new food ingredients may also further move to enable publications that describe the core research studies. Such is the case with sucralose (FCT, 2000).

During the regulatory review process, study designs and data are critically reviewed by expert scientists, in their respective fields, to determine if there is sufficient evidence to establish the safe level of the food additive that can be consumed by the entire population on a daily basis, which is called the acceptable daily intake (ADI). The ADI is based on the No Observed Adverse Effect Level (NOAEL), which is the highest dose that was fed to animals in long-term studies with no toxicological effects. The NOAEL is then divided by a safety factor to ensure the resulting ADI is safe for all potential consumers, including subgroups such as children.

The JECFA first approved sucralose in 1989, after reviewing extensive studies, establishing a temporary ADI of 0–3.5 mg/kg bw/d based on a NOAEL of 750 mg/kg bw/d in a one year study in dogs and a 200 fold safety factor. At that time, the dog study was considered the most appropriate of all the studies to use to establish the ADI. However, further studies were requested, including assessment of safety of long-term consumption by individuals with diabetes. In 1991, following the evaluation of data from additional studies in both animals and humans, the Committee allocated a permanent ADI of 0–15 mg/kg bw/d based on the NOAEL of