Stevia sweeteners: No evidence of genotoxicity

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Researchers at two scientific consulting firms in the United States have conducted a review of published literature on the genotoxicity of steviol glycosides (stevioside and rebaudioside A). They found that the existing studies are robust and do not indicate that steviol glycosides are genotoxic.

Stevia is a herb native to South America, where it has been used as a natural sweetener for hundreds of years. The stevia leaf contains more than 30 steviol glycosides, which are the sweetest components of the leaf. Stevioside and rebaudioside A (Reb A) are the most abundant steviol glycosides and are the most extensively studied. Also, of considerable interest is their metabolite steviol. Due to their intense sweetening properties, steviol glycosides are marketed as low calorie sweeteners in many countries.

The safety of steviol glycosides has been extensively reviewed in the published literature and by national and international food safety bodies. Both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the European Food Safety Authority (EFSA) have reviewed the safety of steviol glycosides on numerous occasions and have established an acceptable daily intake (ADI) of 4 mg per kg body weight per day (based on steviol equivalents). The ADI is a guide to the amount that can be safely consumed on a daily basis throughout a person's life-time. Despite this, two recent publications have expressed concern that steviol glycosides may be mutagenic (i.e. they may change the cells' genetic material) and have called for further genotoxicity studies to complete their safety profiles. Both of these publications cited older studies which were considered by JECFA and EFSA; however, as the issue is persistent in the literature, the authors of this review revisited the genotoxicity studies which are the sources of the continued uncertainty and reviewed additional genotoxicity studies published since 2008.

Genotoxicity of steviol and some of the steviol glycosides have been studied intensely both in vitro and in vivo. Regarding steviol, the majority of in vitro assays have found that it is not genotoxic; however, positive results were found in a forward mutation assay not routinely used in genetic testing using the bacterium Salmonella typhimurium TM677. It has been reported in the literature that the findings from this assay are not appropriate for safety evaluations in humans because of the highly specific bacterial strain (for example this strain is deficient in DNA repair proteins and contains a specific plasmid which makes it more responsive to mutagenic change) and the conditions necessary to reproduce the positive result. Another study showed steviol to be mutagenic in animal cells (Chinese hamster lung cells) in the presence of liver enzymes; however, the high doses of steviol required to cause this effect also induced excessive cytotoxicity (toxicity of the cells) and this has raised a question mark over the validity of the study. Regarding stevioside and Reb A, numerous studies did also not find any evidence for genotoxicity. Only one in vivo study reported that stevioside was genotoxic, i.e. stevioside induced DNA damage in the blood, spleen, liver, and brain cells of rats exposed to stevioside via drinking water (400mg per kg body weight per day). However, the technical conduct and the data interpretation of this study have been the subject of several published critical evaluations.

A review of additional genotoxicity studies published since 2008 found one new set of genotoxicity studies

(in vitro and in vivo assays) on Reb A. No genotoxic effects were found in any of the assays.

This current review concluded that recent suggestions that steviol glycosides present a genotoxic risk to consumers are not supported by actual test results.

For further information, see

Urban JD, Carakostas MC & Brusick DJ. (2012). Steviol glycoside safety: Is the genotoxicity database sufficient? Food and Chemical Toxicology.

EUFIC Information on sweeteners:

Sweeteners