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Health, Bio-Diversity and Organic Farming compromised by Sucralose

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Abstract

Sucralose is a world-wide authorised sweetener that is accumulating in surface waters and is already present in tap water. It was claimed to be safe for human health and not to be metabolised. However, mixture toxicity studies were never performed. Its possible influence on bio-diversity was never studied. Recent literature indicates that sucralose is metabolised in rats and several toxic effects have been described in typical water organisms, but also in rats, mice and humans. As farmers often use surface water, organic farming will come to an end. Clean water is of utmost importance for all living organisms. To protect health and preserve our globe, sucralose should be banned world-wide.

Key words: sucralose; toxicity; ADI; water quality

Introduction

Highlights

- Sucralose is metabolised in rats and the ADI was calculated using a wrong metabolic profile.
- Sucralose should be banned world-wide

What is it all about?

Decennia ago, scientists warned of the global warming. However, as generally known, it was without success as industry and politicians did not take it into account. Now, it seems nearly impossible to limit the warming to 1.5 °C. A less visible problem is the contamination of surface waters with sucralose. Sucralose (Figure 1) is a halogenated table sugar (sucrose) containing 3 chlorine atoms and it belongs to the group of organohalogen components which figure since 1973 in the first group on the black list of Europe (Geuns 2010). These compounds are toxic, have a very long half-life and there is the danger of bio-accumulation. However, in 1991 sucralose was approved for consumption in Canada, in Australia in 1993, in USA in 1998 (Voss et al., 2019). In 1999, sucralose was approved in all food categories in the USA (FDA 1999). Since 2004, sucralose was authorised as a food additive (sweetener) in the EU!

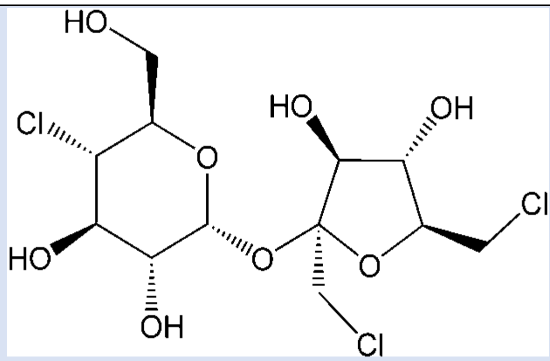

Figure 1: Structure of Sucralose (1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl-4-chloro-4-deoxy-α-D-galactopyranoside

Although only a small amount of sucralose is absorbed and metabolised in the body, the major part is excreted and turns up in the environment. Sucralose is water soluble and cannot be retained by water-treatment plants (van Eyk et al., 2015; Voss et al., 2019; Yang et al., 2021). Therefore, it is not surprising that sucralose has already been found accumulating in fjords in Sweden as early as 2008 (Brorström-Lundén *et al.*, 2008), in surface water and even in tap water in the USA (Voss et al., 2019) and in China (Yang et al., 2021).

Effects of sucralose on water organisms

All water organisms will be in continuous contact with this chlorinated compound and the long-term effect on natural habitats is unknown. It is not known how sucralose influences all these organisms or possibly changes their genomes (mutations), or what the eventual influence is on the food pyramid. Saucedo-Vence et al. (2017) report toxicological hazards induced by sucralose in environmentally relevant concentrations to common carp (*Cyprinus carpio*). They detected sucralose in blood, gills, liver, brain and muscle. No search was done to detect possible metabolites. Sucralose enhanced the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT) and induced oxidative damage of lipids and proteins in different organs: gills, muscle, brain and liver in decreasing order. Abbott and Helbing (2021) studied the influence of sucralose on thyroid hormone (TH) metabolism in premetamorphic American bullfrog tadpoles (*Rana catesbeiana*). The tadpoles were incubated for 48 h in 1, 15 and 32 mg/L sucralose solutions with or without 5 nM thyroxin (T_4). Treatment with only sucralose influenced gene expression in 4 tissues studied: back skin, liver, olfactory epithelium and tail fin. Sucralose also significantly altered gene expression in TH-treated animals. The influence of sucralose on TH signalling is important for all vertebrates including humans as they all depend on TH for maintaining health throughout life. From the above results and the literature cited, it is obvious that sucralose does have an influence on water organisms and if contamination continues might have drastic changes on bio-diversity and eventually on human life.

Influence of sucralose on land organisms and humans

Splitt and Risser (2016) found significant effects of sucralose in the filamentous cyanobacterium *Nostoc punctiforme* in a liquid culture with a hornwort. *Nostoc* forms nitrogen-fixing symbioses with different plants, algae and fungi. The host organism excretes chemo attractants attracting free-living cyanobacteria which form motile filaments, called hormogenia. Once infected, the host plant supplies a hormogonium-repressing factor to maintain the cyanobacteria in a vegetative state, the nitrogen-fixing heterocysts. Sucralose was about 10 times more potent than sucrose in repressing the hormogonia formation and the induction of a polysaccharide sheath essential to establish and maintain the symbiotic state. The heterocyst-forming cyanobacteria (like *Nostoc*) establish nitrogen-fixing symbioses with eukaryotic organisms and contribute to about 50 % of all terrestrial biological nitrogen fixation. This might somehow influence bio-diversity. Palkowska-Goździk et al. (2018) studied the effects of sucralose in male Sprague-Dawley rats. Sucralose lowered thyroid peroxidase, plasma thyroxin (T_4) and thriiodothyronin (T_3) concentrations. Continuous exposure to even low amounts of sucralose might influence human development and health. Bueno-Hernández et al. (2020) performed a chronic randomized, double blind controlled trial with sucralose in young adults. Although some results suggest that chronic consumption of sucralose reduces sensitivity to insulin, the data are not fully convincing as the effects are not increasing with dose. Azad et al. (2020) found clear effects on insulin resistance in the male offspring of sucralose fed female C57BL6J mice. Therefore, Bueno-Hernández et al. should be encouraged to repeat their study as they themselves have reservations about some technical aspects in their study: administration of sucralose should be rather included in gelules, better control and registration of the daily ingestion (e.g., at a fixed time) and provide the same food to all participants.

Azad et al. (2020) studied the effects of non-nutritive sweetener (NNS, aspartame, sucralose) consumption during pregnancy, adiposity and adipocyte differentiation in offspring of humans, mice and pre-adipocyte cells. The child cohort study (N=2298) revealed that children born to mothers regularly consuming NNS had elevated body mass index. The cohort study was supported by a mice study in which maternal NNS consumption caused elevated body weight, adiposity and insulin resistance in the offspring, especially in males. Finally, a study was done with a male 3T3-L1 pre-adipocyte cell line and treatment with 200 nM sucralose at different stages of the differentiation process. A sucralose exposure very early in the differentiation program had the greatest effect on the increase of lipid accumulation in the cells. Also increased was the expression of several transcription factors that convert pre-adipocytes into adipocytes and that have also key roles in the regulation of lipid and glucose metabolism by adipocytes. Sucralose also increased the expression of several genes involved in lipid metabolism. The strength of the study is the triangulating evidence from humans, mice and cultured adipocytes showing that maternal NNS consumption during pregnancy may program obesity risk in the offspring through effects on adiposity and adipocyte differentiation.

Problems due to combustion ovens

It is to be expected that still other problems might arise, because sucralose will sooner or later be found in combustion ovens. Combustion of this sucralose together with other compounds will produce a series of PCB's and dioxins (strongly carcinogenic compounds). Prevention of dioxin formation by incineration at much higher temperatures (1100 °C) compared to the usual 800°C is not a good idea, as then nitrogen from the air is oxidized giving rise to another group of toxins (nitrogen oxides – Nox).

Effects on the ADI (Allowable Daily Intake)

Generally, it is accepted that only a small part of sucralose (± 10 %) is absorbed into the body. Of this, a small amount is metabolised, mainly into its glucuronide (Magnuson et al., 2017). However, Bornemann et al. (2018) found an intestinal metabolism and bio-accumulation of sucralose in adipose tissue in rats. These authors used better extraction and separation techniques than former scientists. The authors also comment on the ADI fixed by U.S. FDA, which was based on a wrong metabolic profile of sucralose in the rat. The ADI in the USA is 5 mg/kg BW, in the EU 15 mg/kg BW. Using the new results obtained in this study would lead to an ADI far below 1 mg/kg/day.

Carcinogenic effects

During a prolonged storing under acid conditions at high temperature (e.g., in soft drinks), sucralose can be degraded into 4-chloro-4-deoxy-galactose (4-CG) and 1,6-dichloro-1,6-dideoxyfructose (1,6-DCF). This last compound is weakly mutagenic both in the Ames assay as well as in the L5178YTK +/- assay. Moreover, sucralose was weakly mutagenic in the mouse lymphoma mutation assay. Earlier, it has already been shown that sucralose damages the DNA of cells of the digestive system as demonstrated by the mouse comet assay (Soffritti et al., 2016). In cell research, van Eyk (2015) found that sucralose and sodium saccharin elicited the greatest degree of DNA fragmentations of all the sweeteners tested in all the cell lines used. Most changes of cell alterations, cell viability and DNA fragmentation were found to be most enhanced in the colon cancer cells. More research should be performed to clarify the mechanisms involved causing these alterations in mammalian cells (van Eyk, 2015).

Soffritti et al. (2016) showed that sucralose was carcinogenic in male animals, mainly in concentrations of 2 and 16 g/L. It has to be taken into consideration that these are rather large concentrations. However, on the other hand, a study by a very large group of independent scientists (Goodson et al., 2015) has shown that compounds that are not carcinogenic on their own can have synergistic reactions when administered together and can induce cancers. As far as we know, this mixture toxicity study has not been performed with sucralose. If we then consider the cola-light products, we see many components that possibly can induce cancers by a synergistic action of weakly carcinogenic compounds (e.g., 4-methyl-imidazole, aspartame and sucralose).

Magnuson et al. (2017) gave a "critical" review on the literature on the safety of sucralose. This review by these 3 food consultants is not as critical as the title suggests. Their conclusion is that sucralose is safe. By considering only GLP (good laboratory practice) research, they seem to forget that thousands of former independent scientists performed fundamental research on different aspects of life which might have led to GLP. They only consider safety to humans, by which possible effects on bio-diversity are neglected. Moreover, their view was not critical enough to see that the analytical techniques used in the absorption, distribution, metabolism, and excretion studies (ADME) lacked thorough extraction knowledge and sufficient separation power as commented by Bornemann et al. (2018). This way, some sucralose metabolites were not detected. Food safety and bio-diversity might be endangered by another definition of GLP: "Great Lobby Problems". In the USA, the Centre for Science in the Public Interest (CSPI) downgraded sucralose from "use with caution" into "avoid" (CSPI, 2016).

Analysis and degradation of sucralose (and derivatives)

Voss et al. (2019) developed an excellent analytical method by silylation derivatization gas chromatography-mass spectrometry using a deuterated internal standard of sucralose. Out of 37

groundwater samples from drinking water wells in California's Central Valley, 13.5 % samples were found to contain sucralose far above the detection limit (21.8 ng/L) with an average value of about 175 ng/L. They cite literature references of samples in Ontario (Canada) taken near to wastewater ponds having a sucralose content up to 24,000 ng/L.
Recently, Yang et al. (2021) could degrade sucralose by ozonation and its degradation products trichloromethane (gaseous), di- and tri-chloro-acetic acid cannot be called harmless to the environment. Moreover, the chemical breakdown will be very expensive. The conclusion of the researchers is that sucralose is a persistent chemical that can influence human wellbeing. Yang et al. (2021) also report that sucralose is not only accumulating in surface waters but it frequently was found in tap water. Sharma et al. (2014) calculated that in 2014 the world production of sucralose was about 3000 ton. Given that nowadays the larger players in food production also use sucralose, it is certainly an underestimation that the last 10 years more than 30,000 tons sucralose are polluting the environment.

Conclusion

The ADI of sucralose is based on a wrong metabolic profile of sucralose in the rat. Using the new results obtained by Bornemann et al. (2018) would lead to an ADI far below 1 mg/kg/day.
Clear-cut harmful effects were observed to the environment and human health.
As many surface waters, used in organic farming, are contaminated by sucralose, organic farming is not possible anymore.
To protect bio-diversity and organic farming and to prevent further damage to all living organisms, sucralose should now be banned world-wide.

Conflict of interest

The author declares that he has no conflict of interest.

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