Polychlorinated dibenzo-p-dioxins and dibenzofurans formed from sucralose at high temperatures

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Sucralose is a widely-used artificial high-intensity sweetener. Although doubts have been raised about the safety of sucralose by several researchers, it can still be found in a broad range of foods and beverages worldwide, including in baked goods. Sucralose may decompose at high temperatures, and participate in chlorination reactions, generating highly toxic compounds. Here, we demonstrate that heating sucralose at high temperatures in stainless steel or other metal utensils in the presence of rust (Al2O3, Fe2O3, and CuO) produces polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs). PCDD/Fs were found in smoke generated during the heating of sucralose and in the residues after heating. CuO enhanced the PCDD/F yield in comparison with Al2O3 and Fe2O3.

Sucralose (4,1′,6′-trichloro-4,1′,6′-trideoxygalactosucrose, TGS) is an artificial sweetener which results from the selective substitution of three of the sucrose hydroxyl groups with chlorine atoms, involving inverting the configuration at the 4-position from the gluco- to the galacto-analogue, resulting in a product 600 times sweeter than sugar1,2. Sucralose is used as a food additive in more than 80 countries, and is present in over 4,000 products, including baked goods3–6. However, several studies have shown that sucralose has metabolic effects that may negatively impact human health7–13. In addition, it has been found that sucralose is not stable at high temperatures14,15.

Using thermoanalytical techniques, Bannach et al. (2009) found that sucralose is thermally stable at temperatures up to 119 °C, but above this temperature, and up to 550 °C, thermal decomposition takes place in three steps without the sucralose melting14. Rahn & Yaylayan (2010) reported that the thermal degradation of sucralose at 250 °C resulted in the generation of toxic chloropropanols15. Our previous studies showed that highly toxic polychlorinated aromatic compounds, such as polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs), dioxin-like polychlorinated biphenyls, and polychlorinated naphthalenes, could be generated during the heating of foodstuffs in the presence of sucralose16–18. It still remains unclear whether these highly toxic compounds could be produced when pure sucralose is heated, and the formation mechanisms for these compounds have not yet been elucidated.

The effects of temperature, utensil materials, and rusts (metal oxides) on the formation of PCDD/Fs when sucralose is heated were investigated in the study presented here. The concentrations of tetra- through octa-chlorinated PCDD/Fs and 17 toxic 2,3,7,8-substituted PCDD/F congeners, collected from the smoke generated by heated sucralose and from the residues after heating, were measured.

Results

Large amounts of sucralose (5 g) were used in the experiments, and the PCDD/Fs produced were quantified. PCDD/Fs were not detected in the smoke or residues when sucralose was heated in quartz, aluminium, or copper utensils (the metal utensils were polished and rust was removed before use) at temperatures between 200 and 400 °C. However, PCDD/Fs were detected in both the smoke and the residues when sucralose was heated at 350°C in stainless steel utensils, and it should be noted that stainless steel is commonly used for cooking utensils.

The PCDD/F concentrations in the smoke and residues were calculated on the basis of the original weight of sucralose (5 g) used in the experiments. Figure 1 shows that the PCDD/F concentrations increased in both the smoke and the residues with increasing temperature. The PCDD/F concentrations were higher in the smoke than in the residues. The total PCDD/F concentrations produced from sucralose (5 g) heated at 400 °C reached $3.1 \times 10^4$ pg g$^{-1}$, which was approximately 25 times higher than the concentrations produced at 350°C. The 17 toxic...
2,3,7,8-substituted PCDD/F congeners contributed approximately 30% of the total amount of PCDD/Fs in the samples.

The surface of metal cooking utensils can become oxidized, so rust, which is composed of metal oxides, is commonly found on utensil surfaces. The effects of different rusts ($\text{Al}_2\text{O}_3$, $\text{Fe}_2\text{O}_3$, and $\text{CuO}$), chosen based on metals typically used for cooking utensils, on PCDD/F formation during the heating of sucralose at 400°C were investigated. Figure 2 shows the PCDD/F concentrations produced in the smoke and residues when sucralose (5 g) was heated in the presence of $\text{Al}_2\text{O}_3$, $\text{Fe}_2\text{O}_3$, and $\text{CuO}$ (1 g) at 400°C. $\text{CuO}$ enhanced the yield of PCDD/Fs in comparison with $\text{Al}_2\text{O}_3$ and $\text{Fe}_2\text{O}_3$. The total PCDD/F concentrations reached $4.2 \times 10^6$ pg g$^{-1}$ when sucralose was heated in the presence of $\text{CuO}$. $\text{Fe}_2\text{O}_3$ also had a strong effect on PCDD/F formation (giving PCDD/F concentrations of up to $1.2 \times 10^6$ pg g$^{-1}$) in comparison with $\text{Al}_2\text{O}_3$ (which gave PCDD/F concentrations of up to $9.7 \times 10^4$ pg g$^{-1}$). PCDD/F concentrations produced when sucralose was heated in the presence of $\text{Al}_2\text{O}_3$, $\text{Fe}_2\text{O}_3$, and $\text{CuO}$ were significantly higher than the concentrations produced when sucralose was heated in stainless steel utensils (which gave PCDD/F concentrations of up to $3.1 \times 10^4$ pg g$^{-1}$). No significant amounts of PCDD/Fs were detected when sucralose was heated at 300°C.

Sucralose (5 g) was heated in the presence of small amounts of $\text{CuO}$ (1 g, 0.1 g, and 0.01 g) at 400°C to study the effects of the amount of metal oxide present on PCDD/F formation. The PCDD/F concentrations in the smoke and residues decreased as the amount of $\text{CuO}$ present decreased. Smaller amounts of sucralose were also tested, and PCDD/F concentrations of approximately $3.0 \times 10^6$ pg g$^{-1}$ were produced from 1 g of sucralose and 0.1 g of $\text{CuO}$ at 400°C.

**Discussion**

The PCDD/F concentrations were higher in the smoke than in the residues (Fig. 1). The PCDD/F distribution agreed with that described in previous reports, the PCDD/Fs produced being mainly in the gas phase. The PCDD/F homologue and congener profiles in the smoke and residues were similar (Fig. 3), but they were different from those observed in previous studies. This indicates that the PCDD/F formation pathways when sucralose is heated could be altered if foodstuffs (e.g., beef and vegetable oil) are added. Foodstuffs could provide a carbon source for the PCDD/F backbone formation. Sucralose was found to mainly act as a chlorine source in previous studies, but it acted as both a chlorine source and a carbon source in
Al2O3 and Fe2O3 were different, the PCDD/F concentrations being found in the residues than in the smoke when CuO was present. and chlorination reactions, called de novo pathways23. The de novo in all cases (Figs. 3 and 4), suggesting that PCDD/Fs might be pro-
acted as catalysts, promoting PCDD/F formation, but did not alter were similar to the PCDD/F profiles formed from sucralose heated in (the Deacon reaction)20, and they found that CuO was the most efficient of the metal oxides that were studied in releasing Cl2 at approximately 375 °C. This reaction would allow Cl2 to be able to participate in the chlorination of aromatic structures, which could then be followed by the formation of dual ring structures in a second metal-catalysed reaction11,22.

Figure 2 also shows that higher concentrations of PCDD/Fs were found in the residues than in the smoke when CuO was present. However, the PCDD/F distributions produced in the presence of Al2O3, and Fe2O3 were different, the PCDD/F concentrations being higher in the smoke than in the residues. We concluded, therefore, that the metal-catalysed PCDD/F formation reaction occurred on the metal oxide surfaces19. The PCDF homologue and congener profiles produced from sucralose heated in the presence of metal oxides were similar to the PCDF profiles formed from sucralose heated in stainless steel utensils (Fig. 4). This suggests that the metal oxides acted as catalysts, promoting PCDD/F formation, but did not alter the PCDD/F formation pathways.

The PCDFs were found at higher concentrations than the PCDDs in all cases (Figs. 3 and 4), suggesting that PCDD/Fs might be produced when a carbon matrix is broken down, in a series of oxidation and chlorination reactions, called de novo pathways25. The de novo synthesis of PCDD/Fs mostly occurred between 200 and 400 °C, giving a PCDF/PCDD ratio of more than one26. It has also been reported that the oxidation of chlorobenzenes (CBzs) produces more PCDFs than PCDDs25. Polycyclic aromatic hydrocarbons (PAHs) and CBzs are considered to be precursors for PCDD/F formation19,26. Although no PAHs or CBzs were detected in the sucralose before it was heated, both PAHs and CBzs were found, along with PCDD/Fs, in the smoke. CBzs were also detected in the residues. This indicates that compounds containing benzene rings can be formed, chlorinated, and oxidized when sucralose is heated in the presence of metal oxides.

The improper use of sucralose at high temperatures may result in human exposure to PCDD/Fs. The study presented here. Furthermore, the addition of foodstuffs could cause PCDD/Fs to be produced at lower temperatures18. CuO was more effective than the other metal oxides as a catalyst for PCDD/F formation19. Sucralose thermally decomposes at 119 °C, liberating HCl14. Hisham and Benson (1995) investigated several metal oxides and found that they could absorb HCl and release Cl2, forming Cl2 with approximately 375 °C. This reaction would allow Cl2 to be able to participate in the chlorination of aromatic structures, which could then be followed by the formation of dual ring structures in a second metal-catalysed reaction11,22.

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Our data indicate that sucralose may produce significant amounts of PCDD/Fs when heated in stainless steel utensils or in metal uten-
sils in the presence of rust (Al2O3, Fe2O3, or CuO) at high temperatures. Occupational exposure to PCDD/Fs has attracted concern17.
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Author contributions
S.D. and G.L. conceived and designed the experiments. S.D. performed the experiments. S.D. and J.H. analysed the data. S.D. wrote and M.Z. reviewed the manuscript.

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