Naturally occurring toxins

In this guide

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Alkaloids

Pyrrolizidine alkaloids

77. Pyrrolizidine alkaloids (PAs) are naturally occurring toxins found in variety of plant species and are produced as a defence mechanism against insect herbivores. *C. sinensis* does not produce PAs itself but depending on their cultivation and harvesting, contamination with other plants (i.e. weeds) that produce PAs is possible.

78. In 2014, the FSA commissioned a research project/market survey of the occurrence of PAs in food (FSA, 2014c). The samples included tea and herbal infusions. The analytical results are provided in Table 1.

Table 1 – Analytical results for PAs detected in tea samples (n=55) (FSA, 2014c).

Sample	Total no. of samples	No. of samples in which PAs were detected	0-100 µg/kg	100-500 µg/kg	500-1000 µg/kg	1000-3000 µg/kg	>3000 µg/kg	Range (µg/kg)
Teas (black, green and Early grey)	55	11	6	4	-	1	-	<LOQ – 1,170

Abbreviations: LOQ – limit of quantification.

79. The findings of the report led to changes in agricultural practices and newer industry results show a reduction in PA levels (FSA, 2014d). The FSA continues to monitor the levels of PAs in food.

80. In 2008, the COT published a statement on PAs in food, specifically in honey and milk (COT, 2008b). The COT noted that the available reports of human poisoning cases did not provide sufficient reliable exposure data to be used in establishing a health-based guidance value (HBGV). The COT therefore concluded that a two-year study in rats administered riddelliine by oral gavage was the most robust basis for assessing the non-cancer effects of PAs (US NTP, 2003). The COT statement does not include any detail on PAs in tea or exposure thereof.

81. In 2011, the EFSA CONTAM Panel assessed the risks related to the presence of PAs in food in feed (EFSA, 2011). Based on the available data, the CONTAM Panel concluded that 1,2-unsaturated PAs may act as genotoxic carcinogens in humans and applied the MOE approach. The occurrence data of PAs was limited to honey, but EFSA concluded that there was a possible health concern for toddlers and children, who were the high consumers of honey.

82. A new exposure assessment including new occurrence data was published by EFSA in 2016 (EFSA, 2016) and was used to update the risk characterisation for the EFSA assessment in 2017 (EFSA, 2017). The assessment considered the presence of PAs in honey, tea, herbal infusions and food

supplements. EFSA established a new Reference Point of 237 µg/kg body weight per day to assess the carcinogenic risks of PAs, and concluded that there is a possible concern for human health related to the exposure to PAs, in particular for frequent and high consumers of tea and herbal infusions.

83. In 2013, the German Federal Institute for Risk Assessment (BfR) published an opinion regarding PAs in herbal teas and tea (BfR, 2013). Green and black tea samples (n=8 each) were analysed for 17 PAs: echimidine, heliotrine, heliotrine-N-oxide intermedine, lasiocarpine, lasiocarpine-N-oxide, lycopsamine, monocrotaline, monocrotalineN-oxide, retrorsine, retrorsine-N-oxide, senecionine, senecionine-N-oxide, seneciphylline, seneciphylline-N-oxide, senkirkine and trichodesmine.

84. The UB value of PA contents in green and black tea was 486.9 and 1155.5 µg/kg of dry product, respectively. While the BfR's exposure assessment did not include green and black tea due to the small number of samples, the BfR overall concluded that the probability of adverse health effects from long-term consumption of teas with high PA contents was "possible" for the general population, pregnant women, breastfeeding women and children; the severity of these adverse health effects may vary. This conclusion was based on "average" robustness of the available data ("some important data is missing or is contradictory"). The BfR recommended that exposures to PAs can be controlled by taking precautionary measures (e.g. vary consumption of herbal teas and teas with other beverages) and/or refraining from consumption.

Tropane alkaloids

85. Tropane alkaloids (TAs) are secondary plant metabolites and are mostly found in high concentrations in the *Solanaceae* and *Erythroxylaceae* plant species. They are characterised by their unique bicyclic tropane ring system and are classed in three major groups: i) hyoscyamine and scopolamine, ii) cocaine and iii) calystegines. Although all TAs have the same basic structure they differ in their biological, chemical and pharmacological properties (Kohnen-Johannsen and Kayser, 2019).

86. In 2017, EFSA commissioned research to obtain representative occurrence data for TAs in foods, to which the FSA provided UK data (FSA, 2017). A total of 286 UK retail samples of which 20 were dry herbal teas were analysed for the EFSA survey, an additional 52 of which 9 were tea were analysed on behalf of the FSA. The TAs tested for were scopolamine, atropine, 6-hydroxytropinone, O-acetylscopolamine, nortropinone, anisodamine, pseudotropine, anisodine,

scopine, apoatropine, scopoline, aposcopolamine, tropine, tropinone, homatropine, 2α-hydroxymethyl, littorine, convolamine, noratropine, convolidine, norscopolamine, convolvine, phenylacetoxytropane, fillalbine, and calystegines (for potatoes and aubergine only).

87. The data reported here focusses on black and green tea samples. For the FSA analysis, samples of black and green tea were selected (n=5 and 4, respectively). Two samples contained low levels of scopolamine at 0.15 µg/kg and 0.05 µg/kg (both in black tea), although this level was below the reporting limit of 0.1 µg/kg and could not be confirmed by ion ratio. The presence of TAs in tea was presumed to be “caused by the unintentional inclusion of TA containing weeds in the tea product.”

88. The FSA research (FSA, 2017) included a review of the toxicity of TAs and concluded that “very little is known about the toxicity of TAs other than atropine and scopolamine.”

89. In 2022, the EFSA published an assessment of the conclusions of the Joint FAO/WHO Expert meeting on tropane alkaloids (EFSA, 2022b). The main TAs considered in the assessments were (-)-hyoscyamine and (-)-scopolamine, which exert their pharmacological and toxicological effects by acting as competitive antagonists of the muscarinic acetylcholine receptors. Both authoritative bodies considered a study in human volunteers as the key study to assess the effects of TAs. The EFSA CONTAM Panel established a group ARfD of 0.016 µg/kg bw for the sum of (-)-hyoscyamine and (-)-scopolamine, based on decreased heart rate. EFSA concluded that “an update the CONTAM Panel assessment on the risks to human health related to the presence of tropane alkaloids in food is not considered necessary.” In contrast, the FAO/WHO concluded that it was not possible to establish an ARfD and instead selected a point of departure of 1.54 µg/kg bw for the sum of the two substances, based on decreased salivary secretion, and applied a MOE approach. For the general diet, MOEs for the general population (children and women of reproductive age) ranged from 3 080 to 3 850 (mean) and 440–616 (95th percentile) for combined exposures to hyoscyamine and scopolamine. These MOEs were not considered to be of concern by the FAO/WHO (FAO and WHO, 2020).

Mycotoxins

90. Mycotoxins are naturally occurring toxins produced by certain moulds (fungi). They grow on a variety of different crops and foodstuffs, often under warm and humid conditions and can cause a variety of adverse health effects and

pose a serious health threat to both humans and livestock (WHO, 2023).

91. Mycotoxins production can occur at any stage during manufacturing, during, cultivation, harvest, processing and storage (Sedova et al., 2018). The literature reports that due to the different processing steps and characteristics of different tea categories (e.g., green and black), fungal contamination likelihoods and varieties differ from each other. Zhang et al., (2022) collated survey results of mycotoxins in different categories. The mycotoxins detected in green and black tea are show in Table 2.

Table 2 – Survey results of mycotoxins in green and black tea (adapted from Zhang et al., 2022).

Tea	Detected mycotoxins
Green	AFB1, ENB, OTA
Black	AFs, AFB1, AFG2, CTN, DON, FB1, OTA, ZEN, T-2

Abbreviations: AFs – Aflatoxins; AFB1 – Alfatoxin B1; AFG2 – Aflatoxin G2; CTN – Citrinin; DON – Deoxynivalenol; ENB – Enniatin B; FB1 – Fumonisin. B1; OTA – Ochratoxin A; ZEN - Zearalenone.

92. In GB, maximum levels for mycotoxin are set in Assimilated Regulation (EU) 1881/2006. While tea is not among the highest-risk commodities for mycotoxins, aflatoxins and ochratoxin A are monitored and regulated. The official methods for sampling and analysis of mycotoxins are listed in Assimilated Regulation (EU) 401/2006.

93. Kyei et al., (2022) investigated the exposure of 439 pregnant women in rural Bangladesh to 35 mycotoxins and their corresponding health risks. Overall, 447 first-morning urine samples were collected from pregnant women and mycotoxin biomarkers were quantified. Median regression analyses were performed to investigate the association between the consumption of certain foods and local stimulants (betel nut/leaf and chewing tobacco), and urinary concentration of frequently occurring mycotoxins. In the tested cohort, 52% of women consumed hot beverages like tea or coffee the day prior to urine collection. While the study did not provide further information on the amounts consumed, it noted that in the region where the study was conducted tea was

consumed more frequently than coffee. The results showed a “significant negative associations between urine OTA concentration and intake of … tea or coffee (p=0.01).” The estimated mean dietary exposure to OTA in the study population (for the total diet, not just from tea) ranged from 400-426 ng/kg bw (LB – UB). The maximum estimated probable daily intake for OTA was 3, 968 ng/kg bw and 8, 070 ng/kg bw when using density-adjusted and creatinine-adjusted data. The health risk was characterised utilising the MOE approach. Even under the LB scenario, the MOEs for OTA were lower than 1000 in nearly all samples (95%) and the authors noted that this indicated a high health concern.

94. Ongoing work of the COT includes the review of the potential risk of several mycotoxins from the diet to maternal health.