Frequently Asked Questions on Pyrrolizidine Alkaloids in Foods

Updated BfR FAQ of 28 September 2016

High levels of 1,2-unsaturated pyrrolizidine alkaloids (PAs) have been detected in teas and herbal teas in the course of various test projects. Higher PA levels can also occur in certain honeys, depending on their origin. In addition to this, one case has occurred in Germany where lettuce was contaminated with plants containing PAs of the genus Senecio (ragwort, groundsel).

As pyrrolizidine alkaloids are undesired in foods and feeds due to their health-damaging potential, the BfR is of the opinion that above all food companies must take measures to lower the contamination of foods with PAs. The BfR has compiled questions and answers on this subject.

What are pyrrolizidine alkaloids?
Pyrrolizidine alkaloids (PAs) are secondary plant ingredients. It is assumed that certain plant species produce these substances to ward off predators. To date, more than 660 different compounds and their N-oxides are known. They have been detected in more than 350 plant species all over the world. Overall, however, when chemotaxonomic considerations are taken into account, it is assumed the PAs occur in over 6000 plant species. Plants containing PAs belong mainly to the Compositae (Asteraceae), coarse-leaf or borage plants (Boraginaeae) and the legume (Fabaceae) families. Examples of indigenous PA-producing plants are common ragwort, common groundsel and viper’s bugloss.

From a chemical point of view, PAs are esters formed from a necine base and aliphatic mono- or dicarboxylic acid (necic acids). In experiments with animals, certain PAs show hepatotoxic as well as carcinogenic and mutagenic effects. This applies to PAs with a 1,2-unsaturated necine structure esterified with at least one branched C5-carboxylic acid. Due to their health-damaging potential, they are undesired in foods and feeds.

Are there any known cases of PA poisoning?
Cases of poisoning are known with animals under such names as “walking disease”, “dunziekte”, “Winton disease”, “Schweinsberger disease” and “Zdar disease”. Liver cirrhosis occurred frequently among other effects in slaughtering cattle fed with hay and silage contaminated with alpine ragwort.

Cases of illness have also been described in the medical literature in humans who ingested high doses of PAs, but there are only a few well documented cases. In most cases, the symptoms affected the liver. In Pakistan, India and Afghanistan, people took ill after eating cereal that had been contaminated with seeds of the Heliotropium and Crotalaria species. In Jamaica, cases of poisoning were caused by so-called bush teas, which contained parts of Crotalaria and ragwort.

Within the scope of “Ärztliche Mitteilungen bei Vergiftungen”, the BfR became aware of an adult who had eaten plant material containing PAs which caused a severe liver function disorder.

What chronic health effects are possible through PAs?
The liver is the primary target organ for PA-related health effects after chronic intake too, but other organs - the lungs in particular - can be affected as well. Certain pyrrolizidine alkaloids proved to be genotoxic carcinogens in animal tests (long-term studies). Animal experiments
and studies with cell models show that above all the metabolites of certain pyrrolizidine alkaloids are responsible for the hepatoxic and genotoxic-carcinogenic effect. Studies with liver cells of humans and rats also indicate that the occurrence of toxic substances during the metabolism of PAs is the same in the cells of rats and humans. This is seen among other aspects as an indication that the results of experiments with rats on carcinogenesis through PAs are also relevant to humans. In toxicological risk assessment, an extrapolation is usually made from results of this kind to the expected effect in humans. There are no epidemiological studies on PA-induced cancer in humans. The embryotoxic effect (toxic effect on the child in the womb) of certain PAs is also known from experiments with animals, but the data situation is unsatisfactory here.

Where does the BfR see a need for research with regard to the toxicological examination of pyrrolizidine alkaloids?

More than 660 different PA compounds and their N-oxides are currently known. It is assumed that at least half of the known PAs have a genotoxic effect. As only a few of the PAs and their N-oxides identified to date however, have been thoroughly examined with regard to their genotoxic-carcinogenic effects, comparative statements on the carcinogenic effects of the individual PAs are not possible at the moment. The BfR sees a need here to conduct additional toxicological tests so that it is possible to differentiate the relative toxicity of the individual PAs. In addition to this, the BfR is pursuing a new approach in order to identify exposure markers in blood and urine which will enable a distinction between carcinogenic and non-carcinogenic PAs. Examinations of this kind, as well as studies to identify and record PA metabolites, are currently one of the areas of main focus of the work undertaken at the BfR.

How can PAs get into foods?

According to the latest level of available knowledge, there are four ways that PAs can find their way into the human food chain:

1. PAs can find their way into food through contamination with PA-forming wild herbs in the cultivation areas of crop plants. Lettuce has been found in Germany that was contaminated with PA-forming ragwort/groundsel. Very high levels of contamination are known to occur in wheat from Afghanistan caused by the severe spread of plants of the genus *Heliotropium* in wheat fields. The PA-contamination of tea and herbal tea varieties is also attributed to contamination of the raw materials which are harvested along with PA-forming weeds in the cultivation areas.

2. Bee products such as honey and pollen can be contaminated with PAs originating from wild plants such as *Echium*, *Senecio* and *Borago* species from which the bees collect contaminated pollen. Raw honeys from certain countries of Central and South America have higher levels compared to those from several European countries.

3. PAs can find their way into food all along the food chain via contaminated feed given to livestock which then passes on to the foods produced by the animals, such as milk and eggs. There are currently no indications, however, that concentrations occur in foods of animal origin which pose a health risk to consumers.

4. The raw materials used in food production originate from plants which produce PAs by themselves. Borage, also known as starflower, which is known to be a PA-forming plant, is used as one of the characteristic herbal ingredients of “Frankfurt Green Sauce”. Dietary supplements (DS) can also be produced on the basis of plants and plant parts or extracts which produce PAs. Capsules are available, for example, which are made from hemp ag-
rimony, a PA-producing plant which belongs to the Compositae family. The PA levels in some of these DS can be very high. No PAs have been found to date in oil-based DS.

Can PAs be easily detected by analytical means?
Due to their great structural diversity and occurrence in a great many different foods, the analysis of PAs poses a special challenge. The BfR has developed special detection methods in recent years and validated them in ring trials. These methods can be used by regional food and feed monitoring authorities and by the food and feed industry. As only a limited number of the PAs that occur are currently available as a reference standard, additional analytical methods were developed at the BfR so that the entire PA content can be estimated.

Are there any foods in which only very small quantities of PAs have been found or none at all?
Within the scope of a current EU project in which the BfR is involved, a very large quantity of data on PA levels in various foods has been collected, with very low PA levels or none at all being found in:

- Yoghurt, cheese (Gouda/Emmental, Brie/Camembert)
- Infant formula (milk powder 0-6 months), follow-on formula (milk powder 6-36 months)
- Beef, pork, poultry meat
- Beef liver, pork liver, chicken liver
- Eggs

Which foods contribute most to PA intake in children and adults?
PA intake in children aged 6 months to 5 years is mainly attributable to herbal teas (incl. rooibos tea), black tea and honey. Apart from certain dietary supplements (DS), a similar pattern can be seen with adults. With adults, the contribution to total PA intake made by honey is lower, and that of green tea higher, than with children. Where levels are high, DS as an additional source of exposure for adults can make a big contribution to total PA intake via food.

Do foods containing PAs pose any health risks to consumers?
The BfR is currently making an assessment of the possible health risks posed by 1,2-unsaturated PAs in foods on the basis of an estimation of total intake using the latest data on the levels contained in the relevant food groups. Accordingly, the PA levels contained in the foods (herbal teas, rooibos tea, black and green tea and honey) could pose a health risk to children and adults if consumed over longer periods (chronic), but there is no acute health risk.

Are there any limit values for PAs in food or regulations to minimise PA levels in food?
No legal limit values currently exist for PAs in foods and feeds, but the Codex Alimentarius Commission has prepared recommendations in a Code of Practice on “Management of the presence of PA-containing plants” and “Control of plant release and spread”.

Within the European Union, the general recommendation applies that exposure to genotoxic and carcinogenic substances should be minimised to the lowest level achievable by reasonable means (ALARA principle: as low as reasonably achievable), as even low intake quantities can result in an increased health risk, especially if consumed regularly. For this reason, the BfR recommends that total exposure to PAs from all foods should be kept as low as possible.
What measures are necessary to lower PA contamination in the view of the BfR?
To minimise possible health risks to high consumers of honey, herbal teas and teas - especially children and expectant and nursing mothers - various measures should be taken to lower the levels in contaminated foods:

- A fundamental prerequisite for the safety of foods is to take great care when cultivating and harvesting the plants that are used to produce tea and herbal tea, as well as lettuce, leaf vegetables and herbs. Because they are so conspicuous, for example, ragwort varieties which can contain PAs are easily recognisable in most cultures, which means that they can be effectively controlled by taking suitable measures.

- Prior to marketing, food companies should continue to make sufficient checks in all affected food categories, especially batches of tea and herbal teas, and investigate the causes of high levels.

- Careful selection of the raw honeys used to make mixed finished produce can contribute to a reduction of PA levels in ready-to-eat honey, for example.

- The BfR supports consistent application of the recommendations made by the Codex Alimentarius Commission which are contained in the Code of Practice on the subjects Management of the presence of PA-containing plants and Control of plant release and spread.

What can consumers do to minimise PA contamination?

- The potential risk for consumers can be reduced if the general recommendation for variety and diversity is heeded when selecting foods. In this way, one-sided contamination with various potentially health-damaging substances, the occasional occurrence of which in small quantities has to be expected in foods, can be prevented.

- Parents in particular are advised not to give their children only teas and herbal teas but also to offer them other drinks, such as water or fruit juice diluted with water. Expectant and nursing mothers should also alternate teas and herbal teas with other beverages. This also applies to people who satisfy their daily liquid requirement mainly in the form of herbal tea.

- As a fundamental principle when preparing salads, leaf vegetables and herbs, plant parts which do not appear to belong to any known edible plants should be removed. The trend, which can be observed in some sectors of the population, of gathering herbs and other plants that grow in the wild in parks, forests and meadows and processing them into salads and green smoothies is viewed critically by the BfR. Special knowledge is required here to avoid PA-containing plants, such as borage, coltsfoot and others.

- People who consume dietary supplements that are based on pollen or PA-producing plants should be aware that these products can contain PAs in high concentrations. This is validated by data provided by the European Food Safety Authority (EFSA).

- According to the latest level of available knowledge, there are currently no indications that PA concentrations occur in foods of animal origin which pose a health risk to consumers.
You will find more information at:

All BfR publications on the subject of PAs
http://www.bfr.bund.de/en/a-z_index/pyrrolizidine_alkaloids-192891.html

BfR Opinion No 030/2016 of 28 September 2016
Pyrrolizidine alkaloids: Levels in foods should continue to be kept as low as possible

Press Release 18/2013, of 15 July 2013
Levels of pyrrolizidine alkaloids in herbal teas and teas are too high
http://www.bfr.bund.de/en/press_releases/2013/18/levels_of_pyrrolizidine_alkaloids_in_herbal_teas_and_teas_are_too_high-187319.html

BfR Opinion No. 018/2013 of 5 July 2013
Pyrrolizidine alkaloids in herbal teas and teas

This text version is a translation of the original German text which is the only legally binding version.