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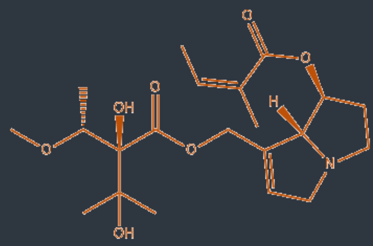
Poison of the month



1,2- unsaturated PA
(Lasiocarpine)

The proposal to designate pyrrolizidine alkaloids (PAs) as the "Poison of the Month" for July...

...came from the Regulatory Toxicology Working Group of the GT (Society of Toxicology), which focuses on the assessment and regulation of health and environmental risks posed by chemicals both from the regulatory and scientific point of view.

The risk of poisoning with pyrrolizidine alkaloids (PAs) due to misidentification or ignorance is particularly high during the summer, when flowers and herbs grow abundantly.

In recent years, food and feed manufacturers have implemented many comprehensive measures to reduce the PA content in commercially available products.

The aim of this article is to raise awareness about the presence of PAs in domestic plants, thereby reducing self-directed intake.

Chemical Structure of PAs

Chemically, PAs are monoesters or diesters of 1-hydroxymethylpyrrolizidine, which is referred to as a necine base. These are esterified with aliphatic mono- or dicarboxylic acids, known as necic acids, with a chain length of 5-10 carbon atoms. Depending on the type and positioning of the esterification(s), various structural types are distinguished. Four basic types are defined based on the saturation level and stereochemistry of the necine base. The 1,2-unsaturated PAs are of the highest toxicological relevance.

PAs in Medicinal Herbs

Some herbs traditionally used as medicinal plants and their teas also contain high levels of PAs. These include lungwort (*Pulmonaria spp.*), coltsfoot (*Tussilago farfara*), common comfrey (*Symphytum officinale*), and butterbur (*Petasites hybridus*).

Pyrrolizidine alkaloids – A Hidden Threat to Your Liver

Pyrrolizidine alkaloids (PAs) are a large group of natural chemical compounds produced by many plants, as well as fungi and bacteria. Naturally, these compounds serve as a defense mechanism against herbivores.

To date, PAs have been detected in over 350 plant species, though it is estimated that more than 6,000 plant species worldwide produce these alkaloid structures. PAs are found in various edible plants commonly used as herbs or in teas. Some of the best-known domestic plants containing PAs belong to the families Asteraceae (*daisies*), Boraginaceae (*borage*), and Fabaceae or Leguminosae (*legumes*).

PAs are primarily ingested through teas (herbal and rooibos tea) and beverages containing herbal tea. Additional intake occurs through the direct consumption of herbs such as borage, oregano, and lovage, or through their use in spices and certain dietary supplements. Despite relatively low consumption quantities, this may significantly contribute to PA exposure. Inadvertently, PAs are also ingested through, for instance, harvested weeds or through misidentification. An important example is common ragwort (*Senecio jacobaea*), which has high PA levels and can be mistaken for arugula during its early growth stage or for St. John's wort when flowering.

PAs are known for their toxic effects on the liver, though not all PAs are equally toxic; specific structural prerequisites are necessary for their toxicity. Depending on their structure, PAs can cause acute and chronic liver damage. Acute and rather unspecific symptoms of PA poisoning include fatigue, abdominal pain, nausea, and in severe cases, jaundice. PA-related poisoning is particularly characterized by veno-occlusive damage to the liver (less commonly to the lungs). Chronic effects of PA poisoning can include liver cirrhosis and liver cancer. The toxicity of these compounds arises from their metabolism in the liver, leading to the formation of reactive intermediates that can damage proteins and DNA. A major challenge in PA poisoning is that symptoms often appear weeks or months after ingestion, complicating proper diagnosis.

Due to their high toxicity, significant efforts have been undertaken in recent years to reduce PA levels in food. As a result, the levels in the primary sources of PA intake have been markedly reduced, thereby lowering the risk for consumers. However, as certain PAs are genotoxic compounds with no safe intake levels, even smallest amounts can pose a potential health hazard, prompting the German Federal Institute for Risk Assessment (BfR) to call for further minimization.

The situation is particularly problematic for pasture livestock, which frequently suffer fatal poisonings. Pasture livestock such as cattle, horses, and sheep ingest large quantities of plant material. This circumstance is exacerbated by the fact that PAs remain toxic in dried form, and thus in hay. Acute poisoning in pasture livestock resembles that in humans. Since the levels of toxic PAs depend not only on the plant itself but also on external factors like weather conditions and soil properties, exact figures cannot be deduced. However, it is estimated that a 1% contamination with common ragwort may be sufficient to deem the harvest hazardous for animals.

Beyond the immediate danger to the animals themselves, PAs can enter the food chain, potentially contaminating animal-derived products such as honey, milk, and eggs. However, current evidence suggests that animal-derived foods do not contain levels that pose a human health risk.

By Ute Haßmann

Literature and links:

- fragen-und-antworten-zu-pyrrolizidinalkaloiden-in-lebensmitteln.pdf
- Risks for human health related to the presence of pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements | EFSA (europa.eu)
- Aktualisierte Risikobewertung zu Gehalten an 1,2-ungesättigten Pyrrolizidinalkaloiden (PA) in Lebensmitteln - Stellungnahme Nr. 026/2020 des BfR vom 17. Juni 2020 (bund.de)
- Foto von Mike Erskine auf Unsplash

1,2-Unsaturated PAs

Structure-activity studies in animal experiments have shown that PAs, in which the necine base has a 1,2-unsaturated necine structure and is esterified with at least one branched necic acid, possess genotoxic (mutagenic) and carcinogenic potential.

Currently, the differences in the carcinogenic potency of individual 1,2-unsaturated PAs are not taken into account in risk assessment; instead, all 1,2-unsaturated PAs are grouped together. To enable a more precise risk assessment, the derivation of potency factors for individual PAs has been proposed, in order to better account for the varying strengths of individual 1,2-unsaturated PAs and their N-oxides in the future. However, the BfR (German Federal Institute for Risk Assessment) considers the existing concepts for this purpose as not yet applicable.

Legally Established Maximum Amount Levels

In the European Union (EU), Regulation (EU) 2020/2040 established maximum levels for PAs in certain foods, effective from July 1, 2022. Foods that exceed the specified limits have since been prohibited from sale in the EU.

However, the general recommendation for all PA-containing foods is to minimize exposure as much as possible, following the ALARA principle (as low as reasonably achievable). The ALARA principle is applied to all genotoxic and carcinogenic substances, as even small amounts, particularly with regular consumption, can increase health risks