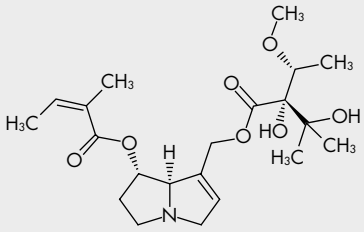
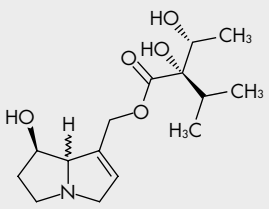
Pyrrolizidine alkaloids

Pure nature – but toxic

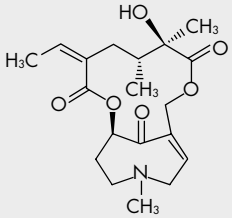
Pyrrolizidine alkaloids (PA) are secondary plant ingredients, of which over 660 different compounds have been detected worldwide in more than 350 plant species. One suspects that plants produce these natural toxins to ward off predators, and assumes that these toxins occur in over 6000 plant species. They belong mainly to the families of the asteraceae, borages and legumes.[1] What is useful for these plants can be dangerous for humans and animals. Many pyrrolizidine alkaloids, primarily 1,2-unsaturated PA, have hepatotoxic, carcinogenic and mutagenic effects. Structurally, these 1,2-unsaturated PA and their N-oxides can be associated with types such as heliotridine, retronecine and otonecine. In turn, these forms can exist as monoesters, open-chain diesters and cyclic diesters (see Figure 1).



Lasiocarpine
(open-chain diester, heliotridine type)



Lycopsamine
(monoester, retronecine type)



Senkirkine
(cyclic diester, otonecine type)

Figure 1: Various structural forms of pyrrolizidine alkaloids (image source: BfR)[2]

How do PA get into food and animal feed?

Wild herbs containing pyrrolizidine alkaloids can thrive on pastures and fields. Examples include the ragwort which is widespread in Europe, the common groundsel and viper's bugloss. In the case of horses and cattle, for example, intake can cause gradual poisoning leading to serious illness or even death.[3] During the harvest of crop plants, wild herbs containing PA can accidentally infiltrate the food chain for humans. Affected, in particular, are herbal teas, rooibos tea, as well as black and green tea. Salads and leafy vegetables are also among the food categories requiring special care during harvest and preparation.[4] If bees ingest nectar or pollen contaminated with PA, the substances can also get into honey. Germany's Federal Institute for Risk Assessment (BfR) asserts that the quantities of PA occurring in the afore-mentioned foods, given prolonged (chronic) intake, can affect the health of children as well as adults.[1]

Sampling

Pyrrolizidine alkaloids are not homogeneously distributed in food, and their sampling requirements are similar to those established for determination of mycotoxins. The EFSA (European Food Safety Authority) and BfR therefore recommend the criteria of (EC) regulation 401/2006, Annex I, E.4 regarding aflatoxin in spices for sampling to determine PA in herbal tea and tea.[5/6]

Analysis

The method of choice is the analysis by means of LC-MS/MS with or without prior solid-phase extraction. It should be noted that only a few of the numerous possible pyrrolizidine alkaloids are currently available as standard substances. The sum of the PA quantifiable with these standard substances are used for assessing health risks. Based on the results of previously analyzed samples, the BfR has issued a preliminary recommendation for examining at least 21 PA (see Table 1).[6] Labor Veritas AG offers examinations of PA by means of LC-MS/MS. In addition to the PA recommended by the BfR, ten additional PA and two tropane alkaloids (TA) are analyzed using this method (see Table 2).

Pyrrolizidine alkaloids and their N-oxides	
Echimidine | Echimidine N-oxide	Retrorsine | Retrorsine N-oxide
Europine | Europine N-oxide	Senecionine | Senecionine N-oxide
Heliotrine | Heliotrine N-oxide	Seneciphylline | Seneciphylline N-oxide
Intermedine | Intermedine N-oxide	Senecivernine | Senecivernine N-oxide
Lasiocarpine | Lasiocarpine N-oxide	Senkirkine
Lycopsamine | Lycopsamine N-oxide	

Table 1: Preliminary selection of 21 PA to be determined in teas

Pyrrolizidine alkaloids and their N-oxides	
7-Acetylintermedine |	Jacobine | Jacobine N-oxide
7-Acetylintermedine N-oxide	Monocrotaline | Monocrotaline N-oxide
7-Acetyllycopsamine	Trichodesmine
Erucifoline | Erucifoline N-oxide	
Tropane alkaloids	
Atropine	Scopolamine

Table 2: PA and tropane alkaloids (TA) analyzed in addition at Labor Veritas AG

Labor Veritas AG possesses many years of experience in analyzing residues of plant raw materials. We look forward to advising you on all issues related to this topic.

Literature, sources

[1] Fragen und Antworten zu Pyrrolizidinalkaloiden in Lebensmitteln, BfR, 2018
[2] Dorina Bodi, Pyrrolizidinalkaloide in Lebens- und Futtermitteln – Herausforderungen an die Analytik, BfR, 2015
[3] Guido Deußing and Ilka Ottleben, Giftkräuter in Lebens- und Futtermitteln analytisch im Griff, Labor Praxis, 2017
[4] Analytik und Toxizität von Pyrrolizidinalkaloiden sowie eine Einschätzung des gesundheitlichen Risikos durch deren Vorkommen in Honig, BfR, Stellungnahme Nr. 38/2011 (ergänzt 2013)
[5] Patrick P. J. Mulder et al., Occurrence of Pyrrolizidine Alkaloids in food, EFSA, 2015
[6] Vorläufige Empfehlung des BfR zur Analytik von Pyrrolizidinalkaloiden (PA) in Kräutertee und Tee (Analytspektrum und Probenahmeverfahren), BfR, Stellungnahme Nr. 2/2016

Contact persons

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Labor Veritas AG, Postfach, CH-8027 Zürich
Phone: 044 283 29 30, Fax: 044 201 42 49
admin@laborveritas.ch, www.laborveritas.ch

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