

## Pyrrolizidine Alkaloids

Pyrrolizidine alkaloids (PAs), sometimes referred to as **necine bases**, are a group of naturally occurring **alkaloids based on the structure of pyrrolizidine**. Pyrrolizidine alkaloids are produced by **plants as a defense mechanism against insect herbivores**. More than 660 PAs and PA N-oxides have been identified in over 6,000 plants, and about half of them exhibit hepatotoxicity.

It has been estimated that **3% of the world's flowering plants** contain pyrrolizidine alkaloids. **Honey** can contain pyrrolizidine alkaloids, as can **grains, milk, offal and eggs**.

### RISK CHARACTERISATION

The target organ for PA toxicity in both experimental animals and humans is the liver. In animals, this toxicity is manifested as anti-mitotic activity leading to extensive fibrosis, nodular regeneration, parenchymal megalocytosis and cancer, while in humans, the major effects are hepatocellular injury, cirrhosis and veno-occlusive disease. At this time, the major toxicological endpoint for humans is considered to be veno-occlusive disease.

On the basis of the limited human data on the incidence of veno-occlusive disease, a tentative NOEL of **10 µg/kg bw/day** is suggested based on the human study reported by Ridker et al (1985). Applying an uncertainty factor of 10 to this figure to take into account individual variation, the provisional tolerable daily intake (PTDI) for PAs is **1 µg/kg bw/day**.

### ANALYSIS

It is known that with the use of the most habitual analytical method for the analysis of pyrrolizidine alkaloids, i.e. **high-performance liquid chromatography – tandem mass spectrometry (HPLC-MS/MS)**, other pyrrolizidine alkaloids might **co-elute** with one or more of the above identified 21 pyrrolizidine alkaloids. In case of co-elution of the following 12 pyrrolizidine alkaloids with one or more of the above identified 21 pyrrolizidine alkaloids, they are included in the sum of 21 pyrrolizidine alkaloids but they are not to be quantified separately.



The possible maximum levels as discussed are lowerbound concentrations. Lowerbound concentrations are calculated on the assumption that all the values of the different individual pyrrolizidine alkaloids (or **"co-eluted"** pyrrolizidine alkaloids) below the limit of quantification are equal to zero.

For tea, herbal infusions, herbs, food supplements containing herbal ingredients, pollen based supplements, pollen and pollen products the Limit of Quantification to be achieved for the individual pyrrolizidine alkaloids (or co-eluted pyrrolizidine alkaloids) is **5 µg/kg**.

(For honey, the Limit of Quantification to be achieved for the individual pyrrolizidine alkaloids (or co-eluted pyrrolizidine alkaloids) is **2 µg/kg**)





## POSSIBLE MAXIMUM LEVELS

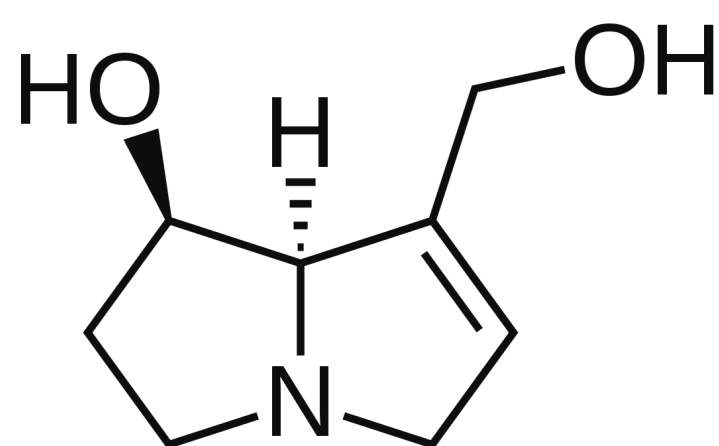
Products	Proposed MRL ( $\mu\text{g/kg}$ )
Herbal infusions – Rooibos	400
Other herbal infusions	300
Herbal infusions – mixtures of rooibos with other herbs	200
Tea ( <i>Camellia sinensis</i> )	100
Herbal tea for infants & young children (solid/ dried product)	7.5
Herbal tea for infants and young children (liquid)	1.0
Food supplements containing herbal ingredients excluding oils	400
Pollen based food supplements	
Pollen and pollen products	
Herbs (fresh, frozen and dried)	400
Cumin seeds (seed spice)	400

**Herbal infusions**– The maximum level of **300  $\mu\text{g/kg}$**  is applicable to mixtures where the relative proportion of the ingredients is not known. In case the relative proportion of the ingredients is known, Article 2 (1) (c) of Regulation (EC) 1881/2006 applies

The possible maximum levels under discussion are based on the occurrence data referred to in the **EFSA scientific report “Dietary exposure assessment to pyrrolizidine alkaloids in the European population”** and more recent data made available to the EFSA database after the publication of the above mentioned scientific report.

Based on these data, the suggested maximum levels for **herbal infusions reflect about the 80th to 90th percentile** of the available data. For tea, the suggested maximum level is above the **95th percentile** of the available data. Taking into account the available information, it is considered that the suggested possible maximum levels are achievable by applying good practices.

In herbs, sometimes very high levels of pyrrolizidine alkaloids are observed in certain herbs such as **borage, lovage, majoram and oregano**. Not considering these very high values the possible maximum level under discussion for herbs reflects the 95th percentile of the available data.



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