Ergot Alkaloids

Occurrence, Toxicity, Analytical Methods, Maximum Levels

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A. What are ergot alkaloids?

Ergot alkaloids (EAs) are a subgroup of the alkaloid family. They are formed naturally by certain fungi, e.g. *Claviceps purpurea*, and primarily occur in ergots. Botanically speaking, ergots are the overwintering form (sclerotium) of the fungus *Claviceps purpurea* which grows on the ovaries of certain types of cereal, forming sclerotia on the caryopses.

History & Etymology

The English term *ergot* is taken from the same French term, meaning "a spur, the extremity of a dead branch", as derived from the Old French term *argot* (12th century, unknown origin), meaning a "cock's spur", describing the shape that the fungus forms on the diseased grain.

The first evidenced occurrence of ergots dates back to the year 600 BC; Assyrian clay tablets described the sclerotia as "harmful formations", explaining why ergot poisonings are also described as the oldest known form of mycotoxicosis.

The first evidenced case of an epidemic-like ergotism occurred in Xanten in 857 AD. In 943 around 40,000 people are estimated to have fallen victim to an ergotism epidemic raging across Europe – predominantly taking its toll in France and Spain. The disease was described as St. Anthony's fire or also as *ignis sacer,* Latin for "holy fire".

In 1938, while conducting pharmaceutical research on ergots, the Swiss chemist Albert Hoffmann synthesised the notorious drug LSD (lysergic acid diethylamide) by chemically changing the structure of lysergic acid amide.

The basic structure of the EAs consists of a tetracyclic ergoline ring system. Depending on the substitution on the C 8 carbon atom, one differentiates between four different EA groups. The formula of the basic ergoline structure is shown in figure 1.

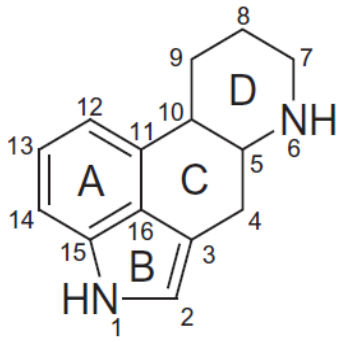

Figure 1: Ergoline ring system

B. How do EAs occur naturally?

EAs are mycotoxins formed by various species of the genus *Claviceps*. In Europe, *Claviceps purpurea* is the most widespread representative of this genus. It particularly infects cereals, mainly rye but also other types of cereal, such as wheat, triticale, barley, millet, and oats. The infection is visible through the formation of so-called sclerotia; characteristically dark-coloured, half-moon-shaped survival stages of the fungus projecting from the husks of the ears of corn.

12 EAs have been identified in the sclerotia of *Claviceps purpurea*, which were subject to scientific evaluation by the European Food Safety Authority (EFSA) in 2012: ergometrine, ergotamine, ergosine, ergocristine, ergocornine, and ergocryptine (consisting of α- and β-isomers) as well as the corresponding forms ending with inine. These EAs, with the exception of the lysergic acid derivative ergometrine, belong to the subgroup of ergopeptines. The forms ending with inine are described as being biologically inactive but are also included in the scientific analysis since processing, for example the baking process, may cause transformations.

C. How do EAs get into foods?

Ergot alkaloids are undesirable in foodstuffs and feedstuffs and occur as a contaminant of the harvesting process. The content of EAs is influenced not only by the climatic conditions but especially also by agricultural measures all along the production chain. This includes selection of the seed stock, cultivation, the selection of raw materials, all the way through to the technological processing of the cereal.

An insufficient removal of ergots prior to processing the cereal can, for example, lead to EA contamination during the grinding process of cereals. However, fragments or ergot-alkaloid-contaminated dust may still lead to EA contamination even after the cereal has been cleaned.

D. Can EAs pose a health risk?

EAs have an impact through their interaction with a series of neurotransmitter receptors, including, among others, adrenergic, dopaminergic, and serotonergic receptors. This kind of interaction can lead to both acute and chronic symptoms in humans. Depending on the intake amount, health impairments may range from slight to severe.

Oral ingestion of low amounts of EAs may cause acute symptoms such as nausea, stomachache, muscle contractions, headaches, cardiovascular problems, and disorders of the central nervous system. Even very low intake amounts may also lead to contractions of the uterus, causing bleedings or a miscarriage.

On consumption of larger amounts, symptoms such as circulatory insufficiencies resulting from the artery-narrowing effects, especially on the heart muscle but also on the kidneys and limbs, have been described. This may lead to hallucinations, cramps and paralyses, all the way through to death caused by respiratory standstill or cardiac arrest.

In 2012, EFSA set an acute reference dose (ARfD) of 1 µg/kg body weight and a maximum tolerable daily intake of 0.6 µg/kg body weight (TDI) for the group of 12 analysed EAs. In doing so, the same toxicological potential was noted for all considered EAs.

The Federal Institute for Risk Assessment (BfR) confirmed these values as an appropriate basis for risk assessments in its

scientific opinion of 7 November 2012. In addition to this, the BfR considers it unlikely that consumption of rye bread containing 59 µg of EAs per kg would result in adverse health impacts. However, a bread containing 585 µg/kg of EAs might cause adverse effects in children aged 2 to under 5 years if medium to large amounts were consumed.

E. How are EAs analysed? / EFSA data gathering process

For analysis of EAs, liquid chromatography is the only separation method described. In the majority of cases, detection is performed using tandem mass spectrometry (QqQ). Fluorescence detection also continues to be used.

The current (2017) data gathering conducted by EFSA (2011 – 2016) covers 6,417 samples, including 4,528 foods from 15 different European countries. Over three quarters of the analysed samples showed no quantifiable levels of EAs. Among the samples containing at least one quantifiable EA, four EAs mostly contribute to the overall content level: ergotamine, ergocristine, ergosine, and ergometrine.

Overall, and also within each analysed food group, the examined rye-containing foods were found to have the highest content levels of ergot alkaloids. However, it was also shown that EA contamination is not only limited to rye and rye-containing products, but also to other cereals such as wheat, spelt, oats, and maize. Nevertheless, the established values were found to be lower on average than in the case of rye products. And no EAs were detected in the examined rice, millet, and buckwheat samples.

EAs were detected in higher amounts in unprocessed agricultural products and in little processed foodstuffs such as grain seeds or flour.

F. Do maximum levels exist for EAs in foodstuffs? Current discussions on maximum levels

Contrary to other mycotoxins (e.g. deoxynivalenol or zearalenone), there are neither national nor European maximum residue levels concerning EAs in cereal-based foods. However, Regulation (EU) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs does indeed set a maximum level of 0.5 g/kg (0.05%) for ergot sclerotia in unprocessed cereals with the exception of maize and rice.

Possible maximum levels for ergot alkaloids are currently being discussed at European level. Nevertheless, the degree of analytical complexity means that, for many products, the analytical questions need to be addressed first. SV