

Ochratoxin A (OTA)

1. Description of substance

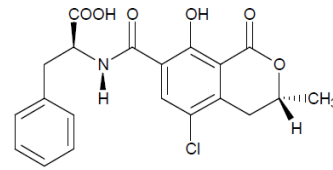
Ochratoxin A (OTA) is a mycotoxin produced mainly by *Aspergillus* molds (such as *Aspergillus ochraceus*) and *Penicillium* molds (such as *Penicillium verrucosum*). It is toxic to the kidney and the liver, etc., of humans and livestock, and is suggested to be related to porcine renal dysfunction in Northern Europe, and in humans to Balkan nephropathy which is an endemic disease in Balkan countries. Its carcinogenicity has been demonstrated in animals but there have not been enough evidences in humans. (1, 2)

Name: ochratoxin A

Molecular formula: $C_{20}H_{18}ClNO_6$

Molecular weight: 403.81

Structural formula



2. Toxicity (from the On-line manual for the diagnosis of livestock poisoning (3))

2.1 Livestock poisoning symptoms

Renal dysfunction such as polyuria, sugar in urine, and proteinuria, and increase in the BUN (blood urea nitrogen) concentration are observed.

Histopathology shows degeneration in proximal tubules, filamentation in the stroma, and hyalinization of the renal glomeruli, etc.

2.2 Mechanism of action

Ochratoxin absorbed into the body is distributed at a high concentration in the kidney. It inhibits the synthesis of proteins, DNA and RNA in the cell. It shows renal toxicity by inhibiting various enzyme activities in the kidney.

It is often detected at the same time with citrinin, mycotoxin similarly with renal toxicity, but there also is a report that additive renal toxicity is not observed by their simultaneous intake. (4)

The rumen of ruminants is highly capable of degrading and converting ochratoxin A into phenylalanine and ochratoxin α with low toxicity, therefore poisoning by ochratoxin is not very much likely to occur; however, calves with immature rumen functions are sensitive to ochratoxin.

2.3 Diagnosis

See the page of fundamentals of diagnosis of poisoning in Livestock Poisoning Diagnostic Manual On-line Version.

3. Contamination in feeds

Aspergillus fungi inhabit from tropical to temperate zones, and *Penicillium* fungi inhabit comparatively cool areas. For that reason, contaminated crops include various species. (2)

Feed materials for which care should be taken due to contamination concentrations and detected concentrations are wheat and barley, etc., maize, and their byproducts. In addition, contamination has been reported for various foods including processed grape products (such as raisins and wine), coffee beans and their processed products (such as instant coffee and canned coffee), processed cacao beans (such as chocolates and cocoa), beer, spices, dried fruits, meat, and milk. Therefore, care should be taken to use their byproducts although they are not frequently used as feed material. (5)

4. Analysis methods

See http://www.famic.go.jp/ffis/oie/sub3/sub3_mycotoxin.html

5. Regulatory situation

There are no regulatory standards designated for both feeds and foods in Japan.

< Risk assessment by JECFA >

Provisional tolerable weekly intake (PTWI) = 100 ng/kg body weight/week (2001)

No observed effect level for deterioration in renal function in a long-term toxicity study in pigs (NOEL): 8 µg/kg body weight/day (5)

6. Monitoring test results etc. in Japan

See http://www.famic.go.jp/ffis/oie/sub2_h21_gaiyou_e.html or http://www.famic.go.jp/ffis/feed/obj/H21FAMIC_monitoring_e.pdf

7. Measures for feed contamination prevention

As expected from the fact that contamination in processed products that undergo the heating process and in beer, etc., ochratoxin A is highly resistant to heat and the fermentation process. Therefore, measures for contamination prevention at the stage of production, storage and transportation of agricultural product are important. Additionally, it has been confirmed that this mycotoxin is transferred to livestock products via feeds, as can be seen by the fact that it also has been detected in meat and milk.

Because ochratoxin A is produced by various molds, different contamination prevention measures are needed by mold kind. Sufficient drying, storage under suitable conditions, and sorting of inferior grains are effective for cereals. Additionally, the Codex committee has prepared the CODEX alimentarius "CODE OF PRACTICE FOR THE PREVENTION AND REDUCTION OF MYCOTOXIN CONTAMINATION IN CEREALS, INCLUDING ANNEXES ON OCHRATOXIN A, ZEARALENONE, FUMONISINS AND TRICOTHECENES." (6)

8. Effects on foods (livestock products) and humans

It has been known that ochratoxin A is transferred to livestock products such as pork and chicken meat via feeds. In some countries, ochratoxin A is detected in porcine blood at a concentration over 50 ppm. As for effects on human health, there is a possibility to cause renal dysfunction, and the relationship with Balkan nephropathy observed in Balkan has been indicated. Ochratoxin A is observed in human blood in many countries, however at a low concentration. There also is a recent

report that ochratoxin A at a higher concentration (mean 18 ± 7 ng/mL) compared to normal persons is detected in the blood from patients with symptoms similar to Balkan nephropathy (Zaied C. *et al.*, *Exp. Toxicol. Pathol.*, 2010) (Tunisia). Moreover, ochratoxin A is found in breast milk and the positive correlation to the intake of foods including pork is indicated (Italy).

9. Reference

- (1) Food and Agricultural Materials Inspection Center, Association of Feed Analysis Methods. 2009. *Methods of Analysis in Feeds and Feed Additives*.
- (2) Japanese Society for Food Hygiene and Safety. 2010. *Encyclopedia of Food Safety*.
- (3) National Institute of Animal Health. 2010. On-line manual for the diagnosis of livestock poisoning.
http://www.naro.affrc.go.jp/org/niah/disease_poisoning/manual/ochratoxin.html (Accessed 27 May 2012)
- (4) Braunberg, R.C. *et al.*: *Nat. Toxins*, 2, 124 (1994).
- (5) Ministry of Agriculture, Forestry and Fisheries (MAFF). 2010. Risk Profile of Ochratoxin A.
http://www.maff.go.jp/j/syouan/seisaku/risk_analysis/priority/pdf/chem_ochratox.pdf (Accessed 27 May 2012)
- (6) CODEX alimentarius. (2003) Code of practice for the prevention and reduction of Mycotoxin contamination in cereals, including annexes on Ochratoxin A, Zearalenone, Fumonisin and Tricothecenes.