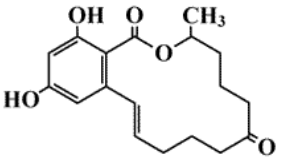
Zearalenone （ZEN)

1. Material Properties

Zearalenone （ZEN）, a common contaminant of all major cereal grains worldwide, is a mycotoxins generated mainly by the Fusarium genus funguses (including *F. graminearum*, *F.culmorum, etc.).* This is a precursor of Zeranol [note] , a growth stimulant for livestock, and is highlighted as one of the endocrine disruptors. It is known that high density of ZEN contained in feed may possibly generate harmful effects such as still-birth and other breeding difficulties, especially for highly sensitive pigs. Contamination with ZEN is mainly found in cereals and also possibly found in grass. Combined contamination with other mycotoxins generated by the Fusarium genus, especially Deoxynivalenol, Nivalenol and Fumonisin is often recognized. (1, 2, 3)

Generic name：Zearalenone
Structural formula
Molecular weight：３１８．４
Molecular formula：$C_{18}H_{12}O_5$



Chemical Structure

Note：The fattening hormones including Zeranol are used in the U.S.A., Canada and Australia, but not in Japan.

2. Toxicity (quoted from “Animal products poisoning Diagnosis Online Manual” (4))

2.1 Symptoms of poisoning for livestock

Symptons of hypertrophied vulva of immature pigs, prolonging estrus cycle for mature pigs, and still-birth of pregnant pigs are found.

Still-birth and estrus symptoms unrelated to ovarian cycle are found.

2.2 Mechanism of action

ZEN acts as agonist for estrogens. ZEN is metabolized by the liver, gastrointestinal mucosa, erythrocyte or intestinal bacteria to be α-zearalenoru and β-zearalenoru. And these substances are further metabolized to be α-zearalenoru and β-zearalenoru. This metabolic reaction greatly varies depending on the animal spice.

The binding activity for the estrogen receptor of rat uterus cytosols functions best in α-zearalenoru, followed by α-zearalenoru, β-zearalenoru, Zearalenone and β-zearalenoru in this order.

2.3 Diagnosis

See the page of fundamentals of diagnosis pf poisoning in Livestock Poisoning Diagnosis Manual Online Version.

3. Contamination of feed

Zearalenone contamination of cereals, including corn and wheat, is spreading throughout the world. Main ingredients on which due considerations should be taken in terms of contamination rate and detection level are corn, wheat, barley, rye, milo, corn gluten feed, corn gluten meal, corn DDGS, screening pellet, wheat bran and oat bran. The residual percentage of zearalenone (ZEN) and its metabolites into animal products is extremely low (1, 3, 5).

4. Analytical method

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

5 Regulation status

[Feeds]

Japan: sets the regulatory value of 1.0 ppm for feed (5).

EU : sets the regulatory value of 20～200μg・kg for feed (1).

＜Risk evaluation by JECFA＞

Provisional tolerable daily intake (PTDI) = 0.5 μg/kg weight/day (1999)

Non-observed effect level (NOEL) when testing swine for 15 days: 40 μg/kg weight/day (1999) (5)

6. Monitoring inspection results 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

Zearalenone (ZEN) is difficult to remove once generated. Because of its high thermal stability, it is important to take measures to prevent contamination for feed in the stage of agricultural production.

The Ministry of Agriculture, Forestry and Fisheries has summarized and revealed “Guideline to reduce contamination of wheat with deoxynivalenol and nivalenol” (6) as a

strategy to remove scab, which will be implemented in the production sites of farmers and related organizations. Codex has also revealed “Code of practice for the prevention and reduction of Mycotoxin contamination in cereals, including annexes on Ochratoxin A, zearalenone, Fumonisin and Trichothecene class)” (7), in which approaches to GAP (Good Agricultural Practices), GMP (Good Manufacturing Practices) and HACCP (Hazard Analysis Critical Control Point) are highly recommended.

8. Influences on food (animal products) and on human

In contamination to food of ZEN, cereals such as corn, barley and wheat, the liver of a pig and chicken and chicken meat are reported.（8） But, the transmission value to an egg and milk of ZEN in feed is low, and the residual level in the possible meal department organization of the domestic animal which ate the contaminated feed in ZEN is low. Therefore, the ZEN contamination level of the livestock is low.

Provisional Maximum Tolerable Daily Intake (PMTDI) is the 0.5μg/kg body weight by JECFA. (8) The IARC Monographs on the Evaluation of Carcinogenic Risks to Human show the scientific evidence indicating the ZEN-related carcinogenicity against a laboratory animal is reported. (9) There is no report of human poisoning case by ZEN. (8)

9. References

(1) “Evaluation of Risk from Fungus Poisoning and International Trends”; Ryoko Konishi, Keiichi Sugiyama; Food Hygienics Journal; 2008

(2) “Feed Analysis Research Standards”; Food and Agricultural Materials Inspection Center; Description o f Feed Analysis; 2009

(3) “Dictionary for Food Safety”; Japan Food Hygiene Association; 2010

(4) “Animal products poisoning Diagnosis Online Manual”; National Institute of Animal Health http://ss.niah.affrc.go.jp/disease/poisoning/manual/zearalenone.html ; Accessed 14 April 2010

(5) “Zearalenone Risk Profile”; Ministry of Agriculture, Forestry and Fisheries （MAFF） http://www.maff.go.jp/j/syouan/seisaku/risk_analysis/priority/pdf/chem_zea.pdf; Accessed 14 April 2010

(6) “Guideline to reduce contamination of wheat with deoxynivalenol and nivalenol”; Ministry of Agriculture, Forestry and Fisheries （MAFF）; 2008

(7) CODEX alimentarius. CODE OF PRACTICE FOR THE PREVENTION AND REDUCTION OF MYCOTOXIN CONTAMINATION IN CEREALS, INCLUDING ANNEXES ON OCHRATOXIN A, ZEARALENONE,

FUMONISINS AND TRICOTHECENES. 2003.
(8) JECFA(2000) Safety evaluation of certain food additives and contaminants. WHO Food Additiv Series: 44.
(9) IARC (1993) IARC Monographs on the Evaluation of Carcinogenic Risks to Human. Vol.56.