

## Natural toxins - a continuous concern

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[www.wur.rikilt.nl](http://www.wur.rikilt.nl)

## RIKILT for Safe Food

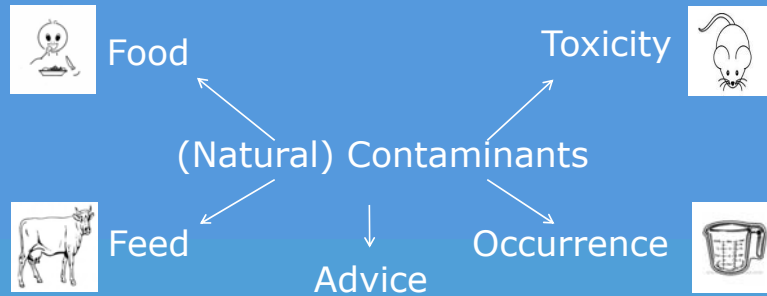
Chemical (bio-)contaminants in food, feed and environment

(mycotoxins, plant toxins, pesticides, dioxins, antibiotics, phycotoxins etc.)

- Part of Wageningen UR
- > 200 employees
- Annual turnover 22 M€



## Natural toxins at RIKILT

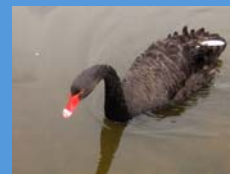


Scientific research on methods development and toxicology  
 NVA and EFSA  
 EU projects  
 Food and Feed Industry



## Natural toxins - a continuous concern

Occurrence of natural toxins often follow the *Black Swan Theory*



An event that is a surprise, has a major effect and after the fact, is often inappropriately rationalized with the benefit of hindsight

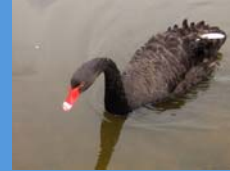
\* As introduced by Mr. Nassim Nicholas Taleb

As presented by Dr. D. Miller at WMFmeetsIUPAC 2012



## Natural toxins - a continuous concern

### *Black Swan Theory – Food Safety*



...as if it *could* have been expected

...relevant data were available but unaccounted for in risk mitigation

...the same for the personal perception (it has never happened before...)

*\* As presented by Dr. D. Miller at WMFmeetsIUPAC 2012*

## Natural toxins - a continuous concern

Risk assessment in food industry often deals with Black Swan events:

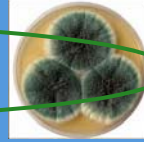
- *Incidents*
- *Are/were relevant data available*
- *Human factor (not to my knowledge..)*

HACCP team must look beyond boundaries e.g. the origin of the product is not only criterium, a history of a 5 year period



## Natural toxins of concern

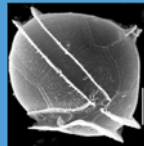
1. Mycotoxins (Fungi)



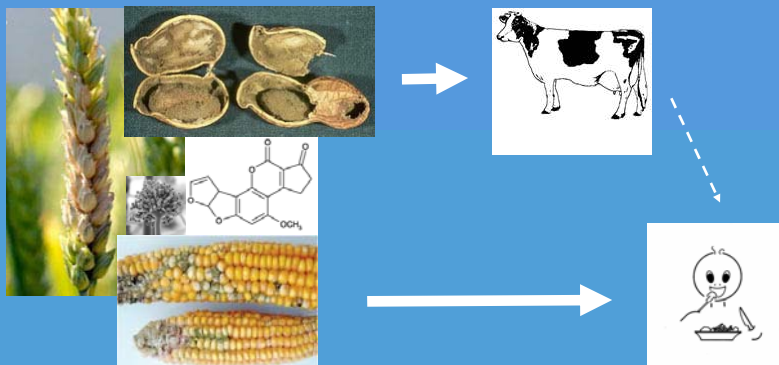
2. Plant toxins (Plants)

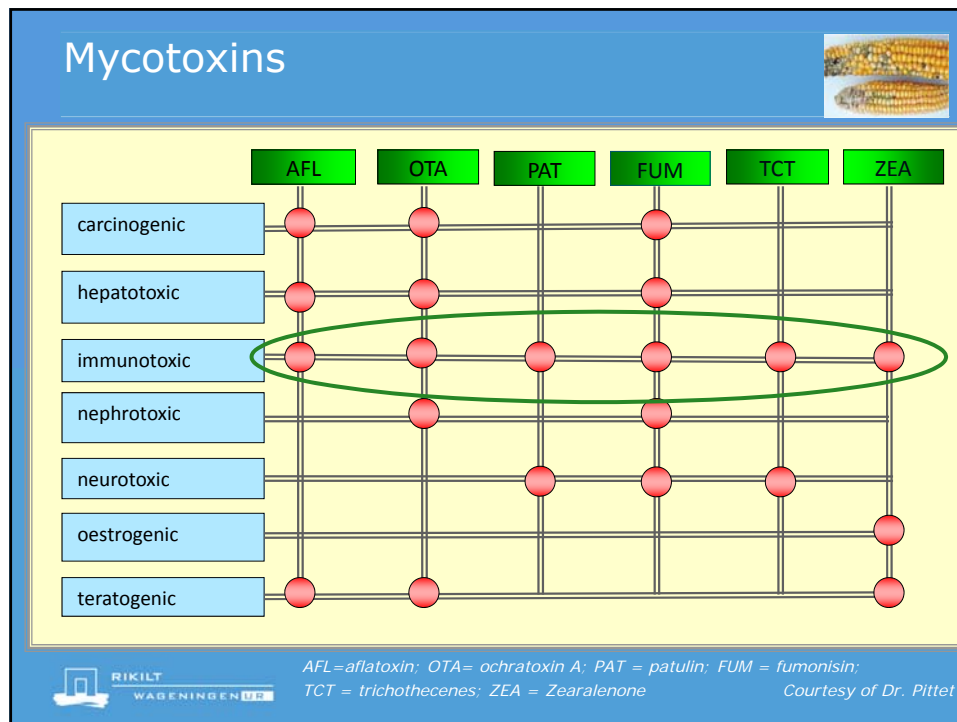


3. Phycotoxins (Algae)




## Mycotoxins - a continuous concern





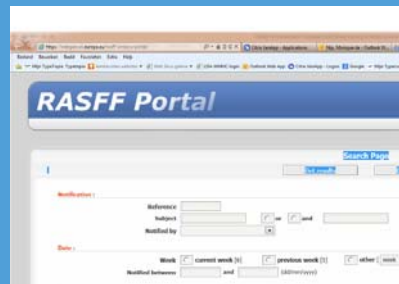
## Mycotoxins – EU Legislation in food

- Commission *Regulation* (EC) No 1831/2003 (and its amendments): Setting maximum levels for certain contaminants in food
 
- Commission *Decision* (EC) No 401/2006 (and its amendments): Laying down the methods of sampling and analysis for the official control of the levels of mycotoxins in food

## Regulations - EU Rapid alert system for food & feed

- Quick information-exchange in the EU on risks to human health;
- MS can identify potential problems and take measures;
- 2011: 635 mycotoxin issues including 514 border rejections

<https://webgate.ec.europa.eu/rasff-window/portal/>



## Mycotoxins - a continuous concern



**994:** Holy fire lysergic acid deriv.  
*C. purpurea*

**1568:** Pieter Brueghel *The Cripples*  
'Holy fire' by ergot alkaloids in **rye**  
(gangrene followed by *necrosis* / *hallucinations*)

**2011:** Ergots in **cereals**; EFSA opinion in 2012  
Regulatory limits on groups of toxins (in addition to ergot sclerotia)



# Mycotoxins – incidents

**Rijst met te veel aflatoxine onderschept**

De Voedsel en Waren Autoriteit (VWA) heeft begin februari de import van 125 ton bruine rijst geweigerd. Uit monitoringbemonsting bleek de rijst te veel aflatoxine te bevatten, een giftig die wordt geproduceerd door schimmels. De VWA heeft een melding naar Brussel verzonden om via het Rapid Alert systeem (het snelle waarschuwingssysteem van de Europese Unie) de andere lidstaten op mogelijke besmettingen te attenderen.

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De besmetting in de bruine rijst liep uit op een waarde van 27 microgram per kilogram. De norm die hiervoor wordt gehanteerd is 5 microgram per kilogram.

Enforcement at EU border diminishes incidents

Climate changes  
Aflatoxin in Italian maize at harvest

World Mycotoxin Journal, November 2008, 1(6): 449-452



Aflatoxin B<sub>1</sub> contamination in maize related to the aridity index in North Italy

F. Battilana<sup>1</sup>, C. Barbano<sup>1</sup> and G. Piva<sup>2</sup>



# Mycotoxins – incidents



Handicraft production / locally sourced food (locatarians):

- Knowledge on contamination routes:
  - New cultivars, susceptible cultivars;
  - Storage of harvested product
  - Origin of raw materials

**Voorraad appelsap toch nog op peil**

De Stator: Gepubliceerd op 23 oktober 2012. Laatste update: 27 oktober, 15:24

Foto: ANP

... van bewerkt  
... van het ... van appels in te leveren, heeft succes geboekt.  
Diverse mensen leverden hun voorraad in bij de producenten ...  
... waardoor het totaal aan appels groeide van duizend naar  
... duizend appels. Een goede basis voor voldoende appelsap voor de ...

- Patulin in handicraft produced apple juice (2009):  
18 of 42 samples > EU regulatory limit 50 µg/l (adult)

Quantification of patulin in Belgium (Gillard et al (2009) WMJ (1) 95-104)

N. Gillard<sup>1</sup>, R. Agneessens<sup>2</sup>, M.L. Dubois

<sup>1</sup>CER Groupe, Division Hormonologie, rue  
Center, rue de Serpont, 100-6800 Libramont

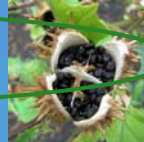


## Natural toxins of concern

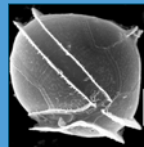
1. Mycotoxins (Fungi)



2. Plant toxins (Plants)



3. Phycotoxins (Algae)



## Plant toxins





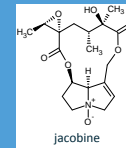
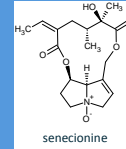
## Plant toxins



Hundreds of plant toxins known

Mostly mentioned:

- PA's: pyrrolizidinealkaloids;
- TA's: tropanealkaloids;
- Aromatic compounds: essential oils; alkenylbenzenes (estragol; methyleugenol; safrol) (herbs);
- Lectins (legumes);
- Furanocoumarins (cruciferous plants);



## Plant toxins – legislation



Food: [37/2010](#) *Aristolochia* spp. (table 2 banned substances, veter. drugs. AO) ;  
[396/2005](#) nicotine, pyrethrins, rotenone, azachdirachtin (MRL pesticides);  
 Feed: [2002/32](#) hydrocyanic acid, gossypol, theobromine, allyl-ITC (glucosinolates);  
 Botanical imp.: weed seeds/fruits met alkaloiden, glucosides, other toxic subst.



2001 kruidenbesluit warenwet (= food) Update will be presented soon  
 - Aristolochic acid must be absent;  
 - Pyrrolizidinealkaloids < 1 µg/kg;  
 - List of plants that are not allowed to be used.



Feed: Pyrrolizidinealkaloids, tropanealkaloids, glucosinolates, opium alkaloids, ...  
 General: safety of botanicals  
 EFSA compendia botanicals

### Other

Codex works on PAs  
 Increased attention/risks:  
 Climate changes => habitat/presence of weeds  
 Quality control of ingredients (gap)  
 Use of herbal preparations to replace antibiotics in feed



## Plant toxins-Incidents



**2008 Afghanistan:** wheat flour contaminated and carry-over to goat milk; 270 persons ill, 50 fatalities due to acute liver failure;

**Cause:** *Heliotropium popovii* H. Riedl subsp. *gillianum* in wheat flour.



## Plant toxins-Incidents

**1990-1991 Belgium:** kidney damage in >100 women (transplantations, cancer)  
**Cause:** Aristolochic acid from *Aristolochia spp* as ingredient in herbal preparations and TCM for slimming

*Aristolochia Clematis*  
(birthwort; pijpbloem)



**2001 Netherlands:** >60 cases of poisoning (epileptic seizures)  
**Cause:** anisatine from ingredient of herbal tea with Japanese star anise instead of Chinese.



## Plant toxins-Incidents



### NACHRICHTEN-ARCHIV

#### Supermarkt: Giftiges Greiskraut im Rucola



In einer Packung Rucola-Salat hat ein Kunde der Discounter-Kette Plus in Hannover nach Medienberichten einzelne Stängel einer giftigen Pflanze entdeckt. Das Gemeine Greiskraut (*Senecio vulgaris*) könne in größeren Mengen mitunter gefährliche Leberschädigungen hervorrufen, schrieb «Spiegel Online». Nach Angaben von Plus-Sprecherin Christina Stylianou sei die betroffene Charge komplett aus dem Sortiment genommen worden, um jedes Risiko auszuschließen. Der Lieferant des Salats sei kontaktiert und um eine stärkere Kontrolle der Lebensmittel gebeten worden.

### 2006 en 2009 Germany:

Weed (*Senecio vulgaris*) in rocket salad <2.5 mg/kg PAs

Issue: pyrrolizidine alkaloids, liver toxicity

⇒ feed: roughage

⇒ food: honey, herbs preparations/TCM



## Plant toxins-Incidents

2010 Netherlands: Alfalfa contaminated with PA producing  
Common groundsel (*Senecio vulgaris*)

- alfalfa grown in areas near the sea
- Used as feed (pellets) for cattle and horses



2010 Toxicity for cows still unknown  
Carry-over of certain PAs to milk is proven

## Plant toxins-Incidents

**2013 Netherlands:** 3 persons hospitalised with severe intoxications after consumption of marshmallow root tea. (a remedy for bile and airway cleaning). However, the tea was made of deadly nightshade, containing atropine.

**Cause:** accidental exchange of dried Marshmallow root (*Althaea officinalis*) for dried deadly nightshade root (*Atropa belladonna* RASFF 2013.0079)



## Natural toxins of concern

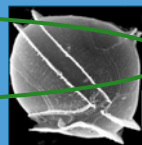
1. Mycotoxins (Fungi)



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3. Phycotoxins (Algae)



## Phycotoxins



Toxins from algae that accumulate in (shell-)fish



## Phycotoxins: "Red tides"

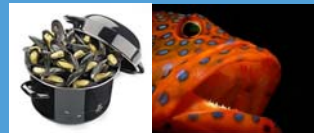
*Explosive growth of algae*



## Phycotoxins



- Paralytic shellfish poisoning-toxins (PSP)
- Diarrhoeic shellfish poisoning-toxins (DSP)
- Amnesic shellfish poisoning-toxins (ASP)
- Azaspiracids (AZA)
- Emerging: palytoxins, brevetoxins, cyclic imines
- Ciguatera toxins



## Phycotoxins



- Several phycotoxin groups EU-regulated
- EFSA: most EU-limits not sufficiently protective; (official) rodent assays inferior
- MBA and RBA for lipophilic toxins will disappear
- Interesting chemical alternatives to MBA e.g. LC-MS/MS explored and validated
- Need for screening methods and (C)RMs

EU regulation using of LC-MS/MS method\* →



*\*Gerssen et al. (2010) In-house validation of a liquid chromatography tandem mass spectrometry method for the analysis of lipophilic marine toxins in shellfish using matrix-matched calibration*

## Phycotoxins - Incidents

**2012 The Netherlands, (August):** A dinoflagellate polluted a Netherlands creek with phycotoxins. An infection of this size was unknown to the Netherlands before.

No human intoxications are known from this incident.



## Phycotoxins - Incidents

**2012 The Netherlands, October 31:** Infected mussels cause a massive outbreak of shellfish poisoning among residents of a retirement home. 100 people fell ill with severe gastro-intestinal problems.

Various fishing areas have been closed and are still closed.

**Suspected cause:** import of infected mussels

**Zeeuwse mosselhandelaar weigert inzicht in handel van ziekmakende mosselen**

Nieuwsbericht Nederlandse Voedsel- en Warenautoriteit | 30 oktober 2012

**100 rusthuisbewoners ziek na eten van mosselen**

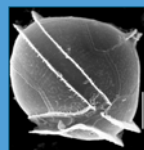


Prins & Diermanse uit Verske wil dat de Nederlandse Voedsel- en Warenautoriteit (NVWA) het bericht rechtzet dat het mosselbedrijf baramette mosselen op de markt heeft gebracht. Dat heeft directeur Anton van Coillie woensdag gezegd. Volgens hem heeft de NVWA de rechtzetting dinsdagavond al bevestigd. Een wondbewoner van de voedselautoriteit ontkent dat.

De NVWA heeft het mosselbedrijf een dwangsom van 80.000 euro opgelegd omdat het weigert informatie te geven over een partij ziekmakende mosselen. Directeur Van Coillie ontkent dat de mosselen afkomstig zijn van Prins & Diermanse.

## Natural toxins of concern

### Discussion



## Natural toxins – Changing world

### Consumers demands:

- healthy ingredients e.g. oats:
  - (re-) introduction of the crop in new areas
  - risks of introduction of toxinogenic fungi
- highly nutritious proteins but no GMO-soy:
  - More legumes e.g. lupin:
    - risks for phomopsin A
    - presence of toxic levels of alkaloids.
- use of herbal preparations, herbal teas and TCM:
  - mix-up causing severe injuries and even deaths
  - unexpected toxic doses
  - specific use by vulnerable groups



## Natural toxins – Changing world

Life cycle:

- The use of crops for biofuel production and the treatment of biofuel raw materials is a challenge for the whole agrichain and needs to be monitored closely
- New in food and feed production in EU is the use of algae for food and feed. This holds the risks for phycotoxins.



## Natural toxins – Conclusions (1/2)

- all these societal trends share the danger of introducing risks formerly unknown to the raw material or to the area.
- what is OK when grown or consumed in one area may be contaminated or overdosed in another area or be contaminated with emerging natural toxins.

## Natural toxins – Conclusions (2/2)

- This forces food safety officers to always be aware of risks of natural toxins in food
- Challenge: incorporate the risk assessment for natural toxins for every link and change in the agrichain
- Use smart and reliable monitoring and work closely with governments, scientists, plant breeders and food suppliers
- Moreover, emerging risks should be detected by using an ERDSS that uses information from inside and outside the food production chain to identify emerging food safety risks

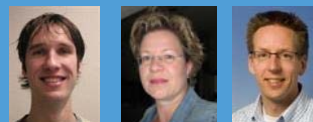


More information on Natural toxins?

Phycotoxins: [Arjen.gerssen@wur.nl](mailto:Arjen.gerssen@wur.nl)

Mycotoxins and Plant toxins: [Monique.denijs@wur.nl](mailto:Monique.denijs@wur.nl)

Program manager Natural toxins: [Hans.mol@wur.nl](mailto:Hans.mol@wur.nl)



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