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International Journal of Food Microbiology 119 (2007) 3 – 10
INTERNATIONAL JOURNAL OF Food Microbiology
www.elsevier.com/locate/ijfoodmicro

Some major mycotoxins and their mycotoxicoses—An overview

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Abstract

Mycotoxins likely have existed for as long as crops have been grown but recognition of the true chemical nature of such entities of fungal metabolism was not known until recent times. Conjecturally, there is historical evidence of their presence back as far as the time reported in the Dead Sea Scrolls. Evidence of their periodic, historical occurrence exists until the recognition of aflatoxins in the early 1960s. At that time mycotoxins were considered as a storage phenomenon whereby grains becoming moldy during storage allowed for the production of these secondary metabolites proven to be toxic when consumed by man and other animals. Subsequently, aflatoxins and mycotoxins of several kinds were found to be formed during development of crop plants in the field. The determination of which of the many known mycotoxins are significant can be based upon their frequency of occurrence and/or the severity of the disease that they produce, especially if they are known to be carcinogenic. Among the mycotoxins fitting into this major group would be the aflatoxins, deoxynivalenol, fumonisins, zearalenone, T-2 toxin, ochratoxin and certain ergot alkaloids. The diseases (mycotoxicoses) caused by these mycotoxins are quite varied and involve a wide range of susceptible animal species including humans. Most of these diseases occur after consumption of mycotoxin contaminated grain or products made from such grains but other routes of exposure exist. The diagnosis of mycotoxicoses may prove to be difficult because of the similarity of signs of disease to those caused by other agents. Therefore, diagnosis of a mycotoxicoses is dependent upon adequate testing for mycotoxins involving sampling, sample preparation and analysis.

Keywords: Mycotoxins; Mycotoxicoses; Aflatoxin(s); Deoxynivalenol; Fumonisins; T-2 toxins; Trichothecenes; Zearalenone; Ergot; Ochratoxin

1. Historical aspects

The toxic secondary metabolites of fungi that we call mycotoxins, have been conjecturally associated with disease, by modern day investigators, and go back to times included in the writings of the Dead Sea Scrolls (noting destruction of "houses of mildew"). They also have been included as the cause of the last of the Ten Plagues of Egypt whereby it was suggested that the oldest son, his family and animals succumbed following the opening of the grain storage facilities whose contents were contaminated by toxic fungi (Marr and Malloy, 1996).

While ergot alkaloids were used as Chinese medicinal preparations over 500 years ago, the accounts of the Middle Ages included descriptions of "St. Anthony's Fire" which was attributed to the human consumption of foods prepared from ergot-contaminated grain. Ergot alkaloids, with both gangrenous and convulsive effects, likely were involved in the "bewitchments" (possession of some evil spirits) leading to the Salem Witchcraft Trials in Salem, Massachusetts.

During the late 1800s and early 1900s there was considerable recognition of the ability of fungi to carry out fermentations and a number of investigators recognized the myriad of "secondary metabolites" produced by fungi in both solid state and liquid fermentations. Because a few of the products of such fermentations were consumed by humans, some interest in the toxicity of these products was developed. DeBary in 1879 noted that when two organisms were grown side by side, one inhibited the growth of the other (Skinner et al., 1947). Other workers followed up with these investigations and Alexander Fleming's discovery of penicillin was a monument to the entire field of antibiosis. Once this discovery was determined to be important, due to the curative effect delivered by this antibiotic for some devastating diseases, the antibiotic industry rapidly developed. Some investigators included studies of animal toxicity during development of antibiotics. Noting that some of these fungal metabolites indeed were toxic to animals was the first clue to many in the scientific community that fungi could produce toxins that could cause disease in humans and other animals.

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doi:10.1016/j.ijfoodmicro.2007.07.019

Concomitant with the studies of grain storage, which included interest in the deterioration of grains by fungi, there became a better understanding of the potential for fungi to be both deleterious to grains in storage and to be agents of toxic problems in livestock and human consumers (Richard, 2000).

During the 1940s and 1950s, episodes of lethal disease in humans in Russia occurred during the early years of the Second World War. This situation was well-documented and referred to as "Alimentary Toxic Aleukia" (ATA). This devastating disease with its necrotizing, hemorrhagic and central nervous system effects, resulting often in death, was recognized as a toxic manifestation of mold contamination of harvested grains (Richard, 2003). However, the true causative toxic compounds were not found at that time and it has retrospectively been considered to be caused by T-2 toxins attributed to the production of this metabolite by *Fusarium sporotrichioides*, the most common fungal isolate from the contaminated grains incriminated in ATA. Simultaneously, the Russians were dealing with another serious disease occurring in both horses and humans. In the 1930s, this disease resulted in the death of thousands of horses. The causative fungus was finally determined to be *Stachybotrys atra*, (now known as *S. chartarum*) but confusion existed due to the similarity of signs of disease to that of ATA. Subsequently, it was found that the chemical nature of the causative compounds of the two diseases is similar and they are known today as members of the class of mycotoxins called trichothecenes. Forgacs and Carll (1962), being convinced that similar diseases occurred in the United States, considered them toxic diseases and began a systematic approach to the study of mycotoxins and mycotoxicoses such as Moldy Corn Toxicosis and Stachybotryotoxicosis (Forgacs, 1962). Also, during this time another disease called facial eczema had plagued the New Zealand sheep industry and was determined to be caused by a toxic component eventually called sporodesmin. It was produced in the conidia of a fungus growing on ryegrass pastures known, at that time, as *Sporodesmium bakeri* (now known as *Pithomyces chartarum*).

Modern mycotoxicology began with the discovery of aflatoxins after losses of a large number of animals in England in 1961 was attributed to consumption of peanut meal incorporated in the diets. Subsequent to the finding of the carcinogenicity of the aflatoxins, the immunosuppressive nature of the aflatoxins and the discovery that the aflatoxins were not only a storage problem in grains but actually contaminated certain crops pre-harvest, the total mycotoxin problem became a multidisciplinary issue involving analytical chemists, microbiologists, agronomists, agricultural engineers, entomologists, plant pathologists, crop breeders, geneticists, medical and veterinary practitioners and producers (farmers/ranchers). The combined efforts of interactions of these groups led to the discovery of many new mycotoxins and their involvement in diseases of animals.

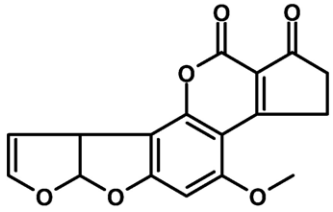

Fig. 1. Structure of aflatoxin B_1 as a representative of the aflatoxins.

Table 1
U.S. Food and Drug Administration action levels for total aflatoxins in food and feed (μg/kg)

Commodity	Concentration
Cottonseed meal as a feed ingredient	300
Corn and peanut products for finishing beef cattle	300
Corn and peanut products for finishing swine	200
Corn and peanut products for breeding beef cattle, swine and mature poultry	100
Corn for immature animals and dairy cattle	20
All products, except milk, designated for humans	20
All other feedstuffs	20
Milk	0.5

2. Mycotoxin/mycotoxicoses overviews

2.1. Aflatoxins

The major aflatoxins consist of aflatoxins B_1, B_2, G_1 and G_2 produced by selected isolates (not all isolates are toxigenic) of either *Aspergillus flavus* or *A. parasiticus* (Fig. 1). However, aflatoxin M_1, a hydroxylated metabolite, found primarily in animal tissues and fluids (milk and urine) as a metabolic product of aflatoxin B_1 should be noted in any discussion of these mycotoxins. Aflatoxin M_1 is not a contaminant of feed grains.

When grain such as corn is growing and there is warm ambient temperature, especially noted during drought conditions, the grain becomes more susceptible to aflatoxin formation. These stresses are more prevalent in the southern United States but they can occur in occasional years in the Midwest (Corn Belt). The saprophytic organism is disseminated via their conidia (asexual spores) carried by wind or insects to the growing crop. Any condition that provides a portal of entry into the host plant tissue or interferes with the integrity of the seed coat allows the organism to enter and grow on the living tissue of the host including the ears or kernels of the developing grain. Insects, such as sap beetles, corn earworms and the European corn borer can provide transmission and portals of entry into the host plant. Corn, peanuts, certain tree nuts and cottonseed are the major U.S. crops affected.

In severely affected crops, yellow–green masses of conidia may be visible at sites of kernel damage or along insect feeding paths. Individual kernels of corn may contain as high as 400,000 μg/kg of aflatoxin (Shotwell et al., 1974), therefore sampling is very important in the testing for levels of contamination in bulk grain lots.

Grains stored under high moisture/humidity (>14%) at warm temperatures (>20 °C) and/or inadequately dried can potentially become contaminated (Ominski et al., 1994). Grains must be kept dry, free of damage and free of insects. These conditions allow mold "hot spots" to occur in the stored grain. Initial growth of fungi in grains can form sufficient moisture from metabolism to allow for further growth and mycotoxin formation.

The aflatoxins are primarily hepatotoxic or cause liver damage in animals; aflatoxin B1 is the most potent. Susceptibility varies with breed, species, age, dose, length of exposure and nutritional status. Aflatoxins may cause decreased production (milk, eggs, weight gains, etc.), are immunosuppressive, carcinogenic, teratogenic and mutagenic (Miller and Wilson, 1994). Aflatoxins can be present in milk of dairy cows, meat of swine or chicken eggs if the animals consume sufficient amounts in their feed. Aflatoxin B_1 is a human carcinogen but may be only part of the total answer to human liver cancer (Robens and Richard, 1992). Pet foods contaminated with aflatoxins have been involved in disease and death of animals consuming sufficiently contaminated food (Garland and Reagor, 2007). Ammoniation and certain adsorbents are effective in reducing or eliminating the effects of aflatoxins in animals (Park et al., 1988). The FDA has action levels for aflatoxins regulating the levels and species to which contaminated feeds may be fed (CAST, 2003) (Table 1). The European Community levels are more restrictive (FAO Food and Nutrition Paper No. 81, 2004) (Tables 2 and 3).

2.2. Deoxynivalenol

Deoxynivalenol (Fig. 2), also known as vomitoxin or DON, is produced principally by *Fusarium graminearum* and in some geographical areas by *F. culmorum* (Richard, 2000). DON may co-exist with zearalenone, another mycotoxin produced by these organisms. DON belongs to the class of mycotoxins called trichothecenes of the Type B group and it is non-fluorescent.

Corn and small grains such as wheat, oats, and barley are the major crops affected but DON can be found in corn as well (CAST, 2003). The organisms survive on residue left on the field from the previous season's crop, providing an inoculum source for the new crop. The organisms do well in cool, moist conditions with contamination of the crop occurring when conidia of the organism are windblown to the corn silks or in small grains to the anthers which emerge outside the floret during anthesis. The fungus penetrates the host ear or floret and produces the disease which may be ear rot in corn or head blight in small grains. Certain environmental conditions may allow for late growing season development of DON in crops. Apparently, DON production is necessary for the organism to produce disease in some crops.

In corn, the ear rot produced by *F. graminearum* may appear. Wheat heads may appear prematurely and unevenly ripe and the kernels will have a blanched appearance (tombstone kernels) at harvest and may have pink staining present as well. In those commodities where there is pink staining the disease may be referred to as pink scab.

Storage under good conditions (<14% moisture), including control of insect pests, will minimize further elaboration of the toxin by these toxigenic fungi. Again, if grains have matured and are stored under appropriate conditions, DON does not further accumulate in storage.

Swine are the animals most usually affected by this toxin and exhibit reduced intake of contaminated grain; if they do eat it they may vomit. Levels above 1 μg/g are considered potentially harmful to these animals (Richard, 1998). Pet foods prepared with wheat contaminated with this toxin have been involved in acute toxicities. DON is immunosuppressive and may cause kidney problems in animals (Pestka and Bondy, 1994). Humans are thought to exhibit a similar vomition syndrome when consuming DON-contaminated grain (Bhat et al., 1989). DON does not appear to be significantly carried over into tissues or fluids of animals consuming toxic levels (Prelusky, 1994). Baking and malting using contaminated wheat and barley are adversely affected (Richard, 2000).

The FDA had issued "Advisory Levels" for the industry (Chesemore, 1993) (Table 4). Again, the European community has more stringent regulations for DON (FAO Food and Nutrition Paper No. 81, 2004) (Table 5).

2.3. Fumonisins

The fumonisins are a group of non-fluorescent mycotoxins (FB_1, FB_2 and FB_3 being the major entities) (Fig. 3) produced primarily by *Fusarium verticillioides* and *F. proliferatum* (CAST, 2003). Strains vary in toxin-producing ability.

Corn is the major commodity affected by this group of toxins although some occurrence has been found in sorghum and rice

Table 2
European Union regulations for aflatoxins (μg/kg)

Human food	AfB1	AfB1, B2, B3, B4	M1
Groundnuts, dried fruit and processed products thereof	2	4	–
Groundnuts subjected to sorting or phys. treating	8	15	–
As above but for nuts and dried fruits	5	10	–
Cereals (including maize) and processed products thereof	2	4	–
Milk	–	–	0.05

Table 3
European Union regulations for aflatoxins (μg/kg)

Feed	AfB1	Feed	AfB1
Feed (exceptions below)	50	Complete feedstuff for pigs and poultry	20
Groundnuts, copra, palm kernel, cottonseed, babasu, maize and products derived from processing thereof	20	Other complete feedstuffs	10
		Complementary feedstuffs for cattle, sheep, goats (except dairy, calves and lambs)	50
Complete dairy feed	5	Complementary feedstuffs for pigs and poultry (except for young animals)	30
Complete feed for lambs and calves	10		

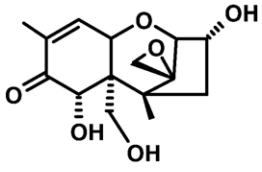

Fig. 2. Structure of deoxynivalenol.

(CAST, 2003). The exact conditions for disease are not known but drought stress followed by warm, wet weather later in the growing season seems to be important. Insect damage to maturing corn ears allows for environmentally present strains of the organism to enter the ear and kernels. However, the organism is present in virtually every seed and is present in the corn plant throughout its growth and therefore is present in the ears and kernels. Sometimes there is considerable amount of fumonisins present in kernels of corn with no symptoms of disease.

While some kernels may have no evidence of infection, other kernels or areas on an ear may exhibit "pink kernel rot" (sometimes may appear white) with closely adhering organism on the kernels. Kernels with insect or bird damage or other broken kernels will often contain the highest levels of toxin. Thus, corn screenings will contain the highest levels of toxins and have been the cause of severe animal disease.

Increase in concentrations of fumonisins during storage does not appear to be a major problem, however, grains should be harvested without additional kernel damage, screened to remove broken kernels and stored dried and maintained at moisture concentrations <14%.

A major disease of horses that includes a softening of the white matter in the brains (leukoencephalomalacia) is caused by the fumonisins (Marasas et al., 1988). Swine lung edema is also produced by the fumonisins (Colvin and Harrison, 1992). Other maladies such as liver disease, including tumors of the liver and kidney, have been noted in studies using rodents. The fumonisins are suspect in the cause of esophageal tumors in certain human populations (Marasas, 1993, 1996). Regardless of the effects on animals, the fumonisins are often involved in liver toxicity and their major mode of action is that they interfere with sphingolipid metabolism. There is no carryover of fumonisins into milk in cattle and there appears to be little absorption of them in tissues (Richard et al., 1996). Because of the lack of toxicity information due to fumonisins in some animal species, disease diagnosis can be difficult.

The guidance levels for fumonisins (total including FB_1, FB_2 and FB_3) in human foods and animal feed proposed by the FDA and European Community are shown in Tables 6 and 7, respectively (FAO Food and Nutrition Paper No. 81, 2004).

2.4. Zearalenone

This mycotoxin was mentioned earlier in that it may co-exist with DON as the same organisms, *F. graminearum* or *F. culmorum* (CAST, 2003), may produce both compounds.

Table 4
U.S. Food and Drug Administration advisory levels for deoxynivalenol in wheat and derived products and other grains (μg/g)

Product	Concentration
Finished wheat products for human consumption	1
Grain and grain by products destined for swine and other animals (except cattle and chickens), not to exceed 20% of diet for swine (40% for other species)	5
Grain and grain byproducts for beef, feedlot cattle older than 4 months and chickens; not to exceed 50% of the diet.	10

Table 5
European Union regulations for deoxynivalenol (μg/kg)

Product	Concentration
Cereal products as consumed and other products at retail stage	500
Flour used as raw material in food products	750

Chemically, it is a phenolic resorcyclic acid lactone (Fig. 4) that is estrogenic when consumed by animals, primarily swine (Hidy et al., 1977). Grains infected with the above organism may exhibit the pink color associated with the production of a pink pigment simultaneously produced with the zearalenone.

Most often this mycotoxin is found in corn. However, it is found also in other important crops such as wheat, barley, sorghum and rye throughout various countries of the world (CAST, 2003). In wheat the conditions for the occurrence of zearalenone would be essentially the same as for the occurrence of DON since the organism gains entry into the host plant in the same manner. Generally, the *Fusarium* species grow in moist cool conditions and similarly invade crops under these more favorable conditions. In wheat, sorghum and corn, zearaleone occurs in pre-harvest grain but in other commodities the surveys are insufficient to determine if zearalenone occurred pre-or post-harvest (WHO Food Additives Series: 44, 2000). Variations in the incidence of zearalenone occur with different crop years, cereal crop and geographical areas.

Again, adequately storing grain to avoid fungal growth is important. However, zearalenone can be formed at relatively cool temperatures and have led to increased levels of this mycotoxin during storage where conditions for fungal growth and mycotoxin formation were favorable.

The most notable effect of zearalenone is that it causes precocious development of mammae and other estrogenic effects in young gilts as well as prepucial enlargement in young barrows. Swine are the most significantly affected species and are considerably more sensitive to zearalenone than, for example, rodents and other species such as cattle and poultry. Weak piglets and small litter size have been attributed to the effects of zearalenone when fed to sows during gestation. Levels of 0.5 to 1.0 μg/g of dietary zearalenone have been associated with the latter effects while hyperestrogenism in swine was associated with dietary levels of 1.5 to 5 μg/g (Prelusky et al., 1994). Zearalenone appears to bind to estrogen receptors and can result in hormonal changes. Mortalities are not a concern due to zearalenone.

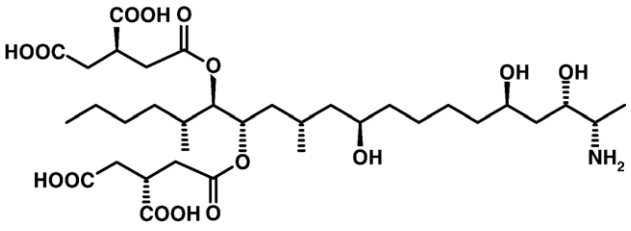

Fig. 3. Structure of fumonisin B_1 as a representative of the fumonisins.

There are no U.S. regulations imposed on the occurrence of this mycotoxin however, the European Union has regulations for this mycotoxin (FAO Food and Nutrition Paper No. 81, 2004) (Table 8).

2.5. T-2 toxin

This mycotoxin is a representative of a large group of mycotoxins called trichothecenes (Fig. 5). It belongs to the Type A chemical class of non-macrocyclic trichothecenes while DON, as mentioned earlier, belongs to the Type B non-macrocyclic trichothecenes. The principle fungus responsible for the production of T-2 toxin is *F. sporotrichioides* (CAST, 2003). Some strains of this fungus also produce some closely related mycotoxins (HT-2 toxin and diacetoxyscirpenol) belonging to the same chemical class.

Corn, wheat, barley, oats, rice, rye and other crops have been reported to contain T-2 toxin (CAST, 2003). Natural occurrence has been reported in Asia, Africa, South America, Europe and North America. Natural levels range from near zero to 10 μg/g with few exceptions up to levels of 40 μg/g. Toxin production is greatest with moisture and temperatures ranging from 6 to 24 °C. Visible evidence of the producing fungus may appear on corn as white mold growth which, in some instances, may appear pink to reddish, often beginning at the tip of the ear.

Adequate storage with low moisture and insect control will minimize further fungal growth and T-2 toxin production. In the United States, T-2 toxin is infrequently found and, if found, likely results from inadequate storage of products.

The major effect of T-2 toxin and other trichothecenes is that they inhibit protein synthesis which is followed by a secondary disruption of DNA and RNA synthesis. It affects the actively dividing cells such as those lining the gastrointestinal tract, skin, lymphoid and erythroid cells. It can decrease antibody levels, immunoglobulins and certain other humoral factors such as cytokines (Niyo et al., 1988; Richard, 1991). The manifestations of disease include signs of weight loss or poor weight gains, bloody diarrhea, dermal necrosis or beak and mouth lesions, hemorrhage and decreased production of milk and eggs. The Type A trichothecenes are more toxic to poultry species than the Type B trichothecenes. Yellow caseous plaques, occurring at the margin of the beak, mucosa of the hard palate, angle of the mouth and tongue, characterize typical oral lesions in poultry. These lesions can occur at dietary levels of 4 mg/kg after one week, 0.4 mg/kg after seven weeks, and with 1–4 mg/kg, beak or oral lesions occurred with concomitant decreased weight and feed intake after three weeks.

No regulations are present for T-2 toxin in commodities or any other products.

Table 6
U.S. Food and Drug Administration guidelines for fumonisins in human foods and animal feeds (μg/g)

	Concentration total fumonisins (FB1, FB2, FB3)
Human foods	
Degermed dry milled corn products	2
Whole/partially degermed dry milled corn product	4
Dry milled corn bran	4
Cleaned corn intended for mass production	4
Cleaned corn intended for popcorn	3
Corn and corn byproducts for animals	
Equids and rabbits	5 <20% diet
Swine and catfish	20 <50% diet
Breeding ruminants, poultry, mink, dairy cattle, laying hens	30 <50% diet
Ruminants >3 mos. before slaughter and mink for pelts	60 <50% diet
Poultry for slaughter	100 <50% diet
All other livestock and pet animals species	10 <50% diet

Table 7
European Union regulations for fumonisins (μg/kg)

Product	Concentration
Unprocessed maize	2000
Maize grits, meal and flour	1000
Maize-based food for direct consumption except maize grits, meal, flour and processed maize-based foods for infants and young children and baby food	400
Processed maize-based foods for infants and young children and baby food	200

2.6. Ochratoxin

Ochratoxin A (Fig. 6) is the major mycotoxin of this group and it is an innately fluorescent compound produced primarily by *Aspergillus ochraceus* and *Penicillium verrucosum* (CAST, 2003). Other fungi such as members of the *Aspergillus niger* group may be important in some commodities or geographic areas (Tjamos et al., 2004).

Little is known of the conditions necessary for involvement of the producing fungi in grains during development in the field. Except for its occurrence in some crops such as grapes, ochratoxin has been regarded as being produced in storage conditions which favor mold growth and toxin production.

Because of the diverse commodities on which the producing organisms and ochratoxin are found, it is difficult to describe the visible presence of the fungus on them. However, visible mold from the major species producing ochratoxin varies from yellowish-tan with *A. ochraceus* to blue–green with *Penicillium* species and black with *A. niger*. Visible mold may not be present for ochratoxin to occur in grains and other commodities. Grain that has a "musty" odor should be suspect for mycotoxins and ochratoxin would be included in the suspect list. Any time the

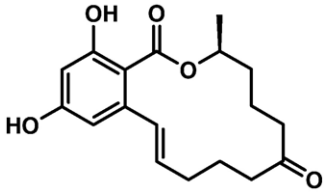

Fig. 4. Structure of zearalenone.

Table 8
European Union regulations for zearalenone (μg/kg)

Product	Concentration
Unprocessed cereals other than maize	100
Unprocessed maize	200
Cereal flour except maize flour	75
Maize flour, meal, grits and refined maize oil	200
Bread, pastries, biscuits, other cereal snacks and breakfast cereals	50
Maize snacks and maize-based breakfast cereals	50
Processed maize-based foods for infants and young children	20
Other processed cereal-based foods for infants and young children and baby food	20

integrity of the seed coat has been compromised there is potential for invasion by ochratoxin-producing fungi. Appropriate sampling for testing is important as "hot spots" can occur in storage. The ubiquitous fungi can contaminate grains stored under high moisture/humidity and warm temperatures. Therefore, grains should be adequately dried and stored where insects are controlled.

Ochratoxin is primarily a kidney toxin but in sufficiently high concentrations it can damage the liver as well. Ochratoxin is a carcinogen in rats and mice and is suspect as the causative agent of human disease. Balkan Endemic Nephropathy is one such kidney disease, often with associated tumors, of humans that is considered by some to be caused by ochratoxin (Pfohl-Leszkowicz et al., 2002). A significant feature of ochratoxin is that it occurs in a wide variety of commodities such as raisins, barley, soy products and coffee in varying amounts but at relatively low levels (CAST, 2003). However, the levels may accumulate in body tissues and fluids of either humans or animals consuming contaminated food because ochratoxin appears to be slowly eliminated from the body. Its occurrence in house dust and other airborne particulates may be of significance in human disease by this mycotoxin (Richard et al., 1999; Skaug et al., 2001). Regulations for ochratoxin A are present in the European Community (FAO Food and Nutrition Paper No. 81, 2004) (Table 9) but none have been established in the United States.

2.7. Ergot

Ergot is often used as a name for any condition which causes for the production or accumulation of ergot alkaloids either in hardened masses of fungal tissue (sclerotia), the most typical association, or liberated into host plant tissue by endophytic fungi. Ergot alkaloids are a large group of compounds produced by fungi that attack a wide variety of grass species, including small grains, during the growing season. They are divided into

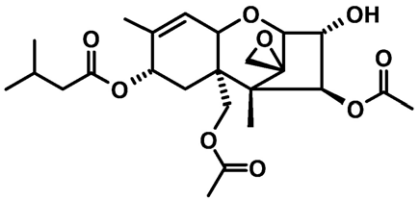

Fig. 5. Structure of T-2 toxin.

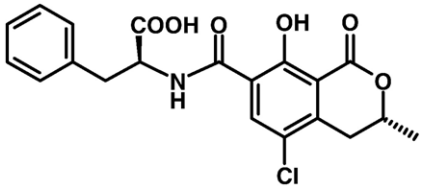

Fig. 6. Structure of ochratoxin A.

the clavine alkaloids, lysergic acids, simple lysergic acid amides and peptide alkaloids (Fig. 7).

The major ergot fungus is *Claviceps* which produces sclerotia in several grass species with *C. purpurea* being the most commonly found species, however, *C. fusiformis* has produced ergot in pearl millet and *C. paspali* has been associated with problems in dallis grass poisonings (CAST, 2003). The endophytic fungi, *Neotyphodium* or *Epichloe* produce ergotpeptines such as ergovaline in tissues of selected grasses such as fescue. In the United States, *Neotyphodium ceonophialum* inhabits tall fescue and produces ergovaline which is implicated in an ergot-like toxicosis in animals grazing on this grass (CAST, 2003).

The entire life cycle of the organism *Claviceps* is quite complex, but for simplicity, species of this genus replace the developing ovaries of the seed with masses of fungal tissue which harden into sclerotia (sometimes called "ergots"). The sclerotia are brown to purple–black in color and contain the ergot alkaloids. The fungus gains entry into the host plant from sclerotia that have been in the soil. The infecting fungal elements (ascospores) are ejected forcibly but also are assisted by wind and splashing rain in gaining access to the host plant where the florets are invaded with subsequent sclerotial development. The sclerotia are harvested with the grain and if not eliminated by screening or some other process they can end up in feed or food made from the contaminated grain.

Noted earlier, ergotism is one of the oldest mycotoxicoses with ancient records of its occurrence. In these cases, signs of gangrene, central nervous system and gastrointestinal effects were observed. Animals are affected similarly. In swine, agalactia has been attributed to ergot alkaloids. The loss of ears and other appendages is a common effect of ergot in animals. Two types of ergotism have been described; gangrenous and convulsive. The differences may be due to the different kinds of alkaloids present in the ergot as variations in amount and kinds of alkaloids can occur in the sclerotia. In more recent years, outbreaks have occurred in human populations and the effects included gangrene and loss of limbs and nervous signs including giddiness, drowsiness, nausea and vomiting (Demeke et al., 1979; Krishnamachari and Bhat,

Table 9
European Union regulations for ochratoxin (μg/kg)

Product	Concentration
Raw cereal grains	5
All products derived from cereals intended for direct human consumption	3
Dried vine fruit (currants, raisins and sultanas)	10

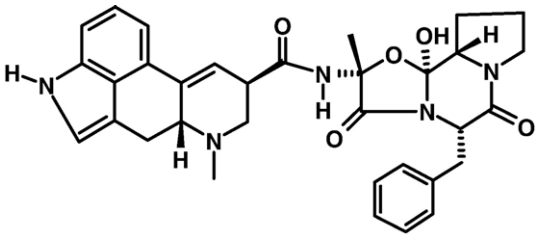

Fig. 7. Structure of ergotamine H as a representative of the ergot alkaloids.

1976). Several different alkaloids were found in these outbreaks. Because some of the ergot alkaloids are vasoconstrictive and have beneficial pharmacological properties, they have been used therapeutically. Fescue toxicity caused by mycotoxins, produced by *N. coenophialum* in the United States, has caused severe economic losses in the beef cattle industry as well as in the dairy and equine industries.

There are no regulatory actions for ergot in grain but the USDA grain grading agency, GIPSA, classifies grain containing 0.05% or more sclerotia as "ergoty."

2.8. Other important mycotoxins

Other mycotoxins such as penitrem (a tremorgenic mycotoxin), patulin, cyclopiazonic acid and citrinin should be classified as important producers of disease in recipient animals including man. They have been found in foods or feeds and have the potential for causing severe disease in animal species. Neither time nor space allows for sufficient discussion of these potential agents of disease. Therefore, the reader is referred to the CAST report (CAST, 2003) for discussions of these mycotoxins.

2.9. Control

A control program for mycotoxins from field to table should involve the criteria of an HACCP approach which will require an understanding of the important aspects of the interactions of the toxigenic fungi with crop plants, the on-farm production and harvest methods for crops, the production of livestock using grains and processed feeds, including diagnostic capabilities for mycotoxicoses, and to the development of processed foods for human consumption as well as understanding the marketing and trade channels including storage and delivery of foods to the consumer's table. A good testing protocol for mycotoxins is necessary to manage all of the control points for finally being able to ensure a food supply free of toxic levels of mycotoxins for the consumer.

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