

Review

The Major Mycotoxins Produced by *Fusarium* Fungi and their Effects

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Abstract

Fungi of the genus *Fusarium* are common plant pathogens occurring worldwide, mainly associated with cereal crops. *Fusarium* species can produce over one hundred secondary metabolites, some of which can unfavourably affect human and animal health. The most important *Fusarium* mycotoxins that can frequently occur at biologically significant concentrations in cereals are fumonisins, zearalenone and trichothecenes (deoxynivalenol, nivalenol and T-2 toxin). *Fusarium* mycotoxins contamination of cereals can cause economic losses at all levels of food and feed production including crop and animal production, and crop processing.

Keywords: *Fusarium*, mycotoxins, trichothecenes, fumonisins, zearalenone.

1. Introduction

Fusarium species are most often encountered as contaminants of cereal grains, oilseeds, and beans. Corn, wheat, barley and products made from these grains are most commonly contaminated although rye, triticale, millet, and oats can also be contaminated. *Fusarium* species can produce over one hundred secondary metabolites, some of which can unfavourably affect human and animal health. The most important *Fusarium* mycotoxins, that can frequently occur at biologically significant concentrations in cereals, are fumonisins, zearalenone and trichothecenes (deoxynivalenol, nivalenol and T-2 toxin).

These compounds can occur naturally in cereals, either individually or as specific clusters of two or more of them depending on the producing fungal species (or strain); they have been implicated (alone or in combination between themselves and/or with other mycotoxins) as the causative agents in a variety of animal diseases and have been associated to some human diseases.

Maize is the crop most susceptible to contamination by all *Fusarium* mycotoxins (particularly important are fumonisins), while wheat and barley are subjected to contamination of deoxynivalenol, nivalenol and, at lesser extent, zearalenone and T-2 toxin and related trichothecenes [1]. The major fungal species (widely distributed in cereal crops) producing these mycotoxins are *F. graminearum*, *F. culmorum* and *F. crookwellense*, producing zearalenone, deoxynivalenol, nivalenol and related trichothecenes, *F. sporotrichioides*, producing T-2 toxin and related trichothecenes, and *F. moniliforme* and *F. proliferatum*, producing fumonisins.

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Mycotoxin contamination of crops may cause economic losses at all levels of food and feed production including crop and animal production. Contaminated grains result in increased costs for handlers and distributors due to extra drying costs, excess storage capacity, losses in transit, loss in markets. The occurrence of mycotoxins varies from commodity to commodity, year to year, and region to region. Years of environmental conditions favorable to mycotoxin development will result in higher economic losses. *F. graminearum* is the primary causal agent of wheat head scab and causes extensive damage to wheat in humid and semihumid wheat growing areas of the world by reducing grain yield and quality [1].

2. Particularities of Concerned Mycotoxins

Trichothecenes

The trichothecenes constitute a family of more than sixty metabolites produced by a number of fungal genera, including *Fusarium*, *Myrothecium*, *Phomopsis*, *Stachybotrys*, *Trichoderma*, *Trichothecium*, and others [2].

The trichothecene mycotoxins have been isolated and found in Canada, England, Japan, South Africa, and the United States.

The most common mycotoxins in the trichothecene family found in grain are DON and T-2, with ZEN and Fumonisin also commonly found [4]. *Fusarium graminearum*, the parent fungi that produces DON, causes both Gibberella Ear Rot in corn, and head scab in wheat.

Over a ten year period the Mycotoxin Laboratory at North Carolina State University found *Fusarium* species of fungi in almost every lot of corn tested. DON was detected in over 60 percent of poultry and dairy feed tested, and ZEN was found in 15 to 20 percent of feeds tested. The *Fusarium* species of fungi are capable of producing 70 different mycotoxins, with some species producing as many as 17 strains of mycotoxins simultaneously. Fumonisin is a recent discovery that research indicates is very toxic to horses, but little is known of its incidence or range [8].

Health Hazards. The trichothecene family of mycotoxins affects each species of animals in different ways.

Testing done so far indicates that poultry has the highest resistance to these toxins.

Cattle, sheep, and goats have some level of resistance due to their multiple digestive process, while animals of the monogastric digestive process seem to have the least resistance to the toxins.

Swine seem to be the most sensitive, partly due to their increased sense of smell which leads to feed refusal [5].

The greatest problems associated with these toxins are from prolonged feed intake at low contamination levels.

The effects depend on the specific toxin, the duration of exposure, and the type of animal involved. All animal species suffering from chronic toxicoses show very good to excellent signs of improvement when the contaminated feed is removed. Few long term side effects remain with most of this group of toxins if diagnosis is made quickly before the general health of the affected animals is compromised [4].

The processing of grain with toxins in the trichothecene group generally does little to remove the toxin. Milling, baking or boiling has only a slight effect in removing the toxins. Tests conducted on finished products contaminated with these mycotoxins have shown that 50 to 60 percent of the toxins are transmitted to the finished product. In some cases, such as the tempering of grain to reach a desired moisture level, the toxins have actually increased due to the proper environmental conditions needed for toxin production. The toxins can be transmitted to final products such as flour, bread, crackers, and cereal [4].

Deoxynivalenol (DON)

Pathogen. *Fusarium graminearum* is the parent fungi of deoxynivalenol (DON) or vomitoxin. Wheat and barley are the most commonly effected grain crops but the same fungus does infect corn.

In the field, it shows up as a brown discoloration at the base of barley glumes, a pink to reddish mold on the glumes and kernels of the wheat heads and the tips of the ears of corn. Spores from the mold stage of the fungi can stay dormant on infected residues left on or in the soil. Contamination is most severe in fields where corn follows corn, or where corn follows wheat, especially if the previous crop was infected [6].

Ecology. The optimal temperature range for the DON mold is 70 to 85 F with moisture levels preferred to be greater than 20 percent. There are exceptions to be noted.

The mold can survive temperatures as low as 0 F for short periods of time. This particular fungi has two distinct growth cycles, with the mold growing during the warm temperatures of daytime, while the toxins are produced during the cooler temperatures of the night [3].

Health Effects. The symptoms associated with DON poisoning are many and varied which sometimes leads to its misdiagnosis as a problem. At low levels of toxicoses the symptoms may include behavioral and skin irritations, feed refusal, lack of appetite, and vomiting. In later stages, symptoms may include hemorrhage and necrosis of the digestive tract, neural problems, suppression of the immune system, lack of blood production in the bone marrow and spleen, and possible reproductive problems including birth defects and abortion [5, 8].

Zearalenone (ZEN)

Phatogen. Zearalenone is very similar to deoxynivalenol (DON) in most aspects with a few exceptions. The zearalenones are biosynthesized by *Fusarium graminearum*, *Fusarium culmorum*, *Fusarium equiseti*, and *Fusarium crookwellense*. All these species are regular contaminants of cereal crops worldwide [2].

Ecology. The growing conditions of ZEN are very comparable to DON, with the optimal temperature range of 65E to 85E F. A drop in temperature during growth also stimulates the production of toxins [3]. The moisture content required by ZEN is also similar to DON at 20 percent or greater.

But if the moisture content during growth drops below 15 percent the production of toxins is halted. This is one of the reasons that corn for storage must be dried to moisture levels less than 15 percent [6].

Health Effects. The greatest difference between ZEN and DON is the way the toxin acts in animals. ZEN mimics the hormone estrogen in the way it effects animal tissue. Swine are the most sensitive to its effects with levels of 1 ppm causing feed refusal.

Continued consumption of contaminated grain will cause estrogenism (health problems related to the reproductive system).

These effects include swelling of the reproductive organs including the genital and mammary glands, interruption of the reproductive cycles, birth defects, and atrophy of the ovaries and testes. In male animals, feminization occurs with enlargement of the mammary glands and loss of sex drive [8, 3].

Poultry show little or no effects from ZEN consumption. Cattle also show very little effect except in cases of prolonged consumption of high levels (greater than 15 ppm) of ZEN.

The effects produced are reduced milk production, swollen reproductive organs, and in some cases infertility. The ZEN is passed through

the system with very little absorption shown in milk, urine, or body tissues [3].

Fumonisin

Phatogen. Fumonisin are produced by a number of *Fusarium* species, notably *Fusarium verticillioides* (formerly *Fusarium moniliforme* = *Gibberella fujikuroi*), *Fusarium proliferatum*, and *Fusarium nygamai* [2]. These fungi are taxonomically challenging, with a complex and rapidly changing nomenclature [2].

The major species of economic importance is *Fusarium verticillioides*, which grows as a corn endophyte in both vegetative and reproductive tissues, often without causing disease symptoms in the plant. However, when weather conditions, insect damage, and the appropriate fungal and plant genotype are present, it can cause seedling blight, stalk rot, and ear rot. *Fusarium verticillioides* is present in virtually all corn samples.

Most strains do not produce the toxin, so the presence of the fungus does not necessarily mean that fumonisin is also present. Although it is phytotoxic, fumonisin B1 is not required for plant pathogenesis [2].

The mold appears on the corn ears as a cottony white to light grey filaments between the corn kernels. As the mold progresses the kernels will turn grey to light brown.

The fumonisin toxin can grow in the kernels even with no apparent outward signs of mold.

Testing of the grain is the only positive means of verifying whether fumonisin is present or not [6].

Ecology. Growing conditions vary widely. The temperature and moisture ranges are so wide spread as to include most of the Northern and Southern Hemispheres.

The one common factor associated with fumonisin is that higher incidence of infections seem to occur after periods of drought which stress the plants immune system [6].

Fumonisin causes the corn kernels to become brittle and crack more frequently than is normal. The more the grain is handled the more cracking and breaking occurs, giving the fungi more host material to grow on.

For this reason corn screenings should be very suspect when used as feed, especially in horses. Testing has shown that screenings contain a higher level of fumonisin toxin (and mycotoxins in general) than the whole grain product [6].

Health Effects. Fumonisin affect animals in different ways by interfering with sphingolipid metabolism. They cause leukoencephalomalacia (hole in the head syndrome) in equines and rabbits; pulmonary edema and hydrothorax in swine; and

hepatotoxic and carcinogenic effects and apoptosis in the liver of rats. In humans, there is a probable link with esophageal cancer [2].

The occurrence of fumonisin B1 is correlated with the occurrence of a higher incidence of esophageal cancer in regions of Transkei (South Africa), China, and northeast Italy. It has been isolated at high levels in corn meal and corn grits, including seven samples from a supermarket in Charleston, S.C., a city which has the highest incidence of esophageal cancer among African-Americans in the United States. Several other mycotoxins, nutritional parameters, and other factors have also been implicated in the etiology of human esophageal cancer [2].

A possible case of acute exposure to fumonisin B1 involved 27 villages in India, where consumption of unleavened bread made from moldy sorghum or corn caused transient abdominal pain, borborygmus, and diarrhea. All those affected recovered fully.

Finally, fumonisins can cause neural tube defects in experimental animals and thus may also have a role in human cases. It has been hypothesized that a cluster of anencephaly and spina bifida cases in southern Texas may have been related to fumonisins in corn products.

The International Agency for Research on Cancer has evaluated the cancer risk of fumonisins to humans and classified them as group 2B (probably carcinogenic). Unlike most known mycotoxins, which are soluble in organic solvents, fumonisins are hydrophilic.

This makes them difficult to study. Usually they are extracted in aqueous methanol or aqueous acetonitrile.

High - performance liquid chromatography with fluorescent detection is the most widely used analytic method. The fumonisin story raises the specter that there may be many other occult but toxic products of fungal metabolism that have not yet been discovered because of their hydrophilic nature [2].

Nivalenol (NIV)

Pathogen. Nivalenol is produced by the *Fusarium nivale* fungi and has recently been isolated. Little is known of its growth cycle or habitat range. Studies have shown it to be much rarer in occurrence and has only been found in a few samples of barley, wheat, wheat flour, and rice [4].

Health Effects. Though little actual test data has been produced, the results so far cause scientists to be extremely cautious. Preliminary testing shows that NIV is thought to be 10 times more potent than DON. If the advisory level for Don is used as a

guide for toxicity, NIV would have an advisory level of only 0.2 ppm [4].

T-2 Toxin

Pathogen. *Fusarium sporotrichioides* and some strains of *F. roseum* produce T-2. T-2 has been found in corn in the field, silage, and prepared feeds made with corn.

Health Effects. During WWII, a very severe human disease occurred in the former Soviet Union. Alimentary toxic aleukia (ATA) is believed to have been caused by T-2 and HT-2 in grain left to overwinter in the field. When this grain was consumed, severe mycotoxicosis occurred. ATA results in a burning sensation in the mouth, tongue, esophagus, and stomach.

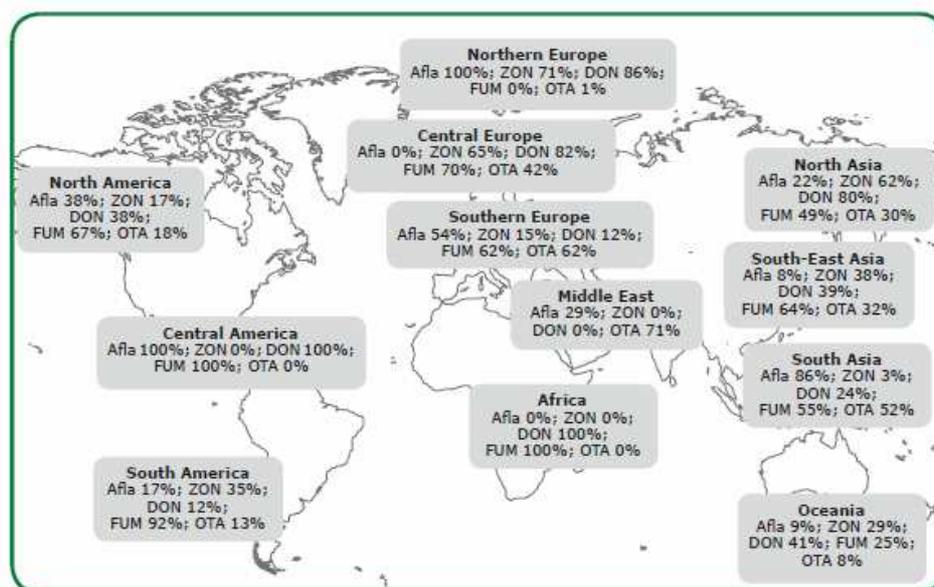
Eventually the blood making capacity of the bone marrow is destroyed and anemia develops. In the final stages hemorrhaging of the nose, gums, stomach, and intestines develops and the mortality rate is high. In poultry, T-2 may produce lesions at the edges of the beaks, abnormal feathering, reduced egg production, eggs with thin shells, reduced body weight gain, and mortality [2].

According to data presented by BIOMIN, the leader in Mycotoxin Risk Management, results of mycotoxin analyses for the second quarter of 2011 show that in the period between April and June 2011, a total of 804 samples were analysed and 2867 analyses were carried out for the most important mycotoxins in terms of agriculture and animal production – aflatoxins (Afla), zearalenone (ZON), deoxynivalenol (DON), fumonisins (FUM) and ochratoxin A (OTA). Samples originated from different regions: America (North, Central and South), Asia (South-East, South and North), Oceania and Europe (Northern, Central and Southern) and the Middle East and Africa. Samples tested were diverse, ranging from cereals such as corn, wheat, barley and rice to processing by-products, namely soybean meal, corn gluten meal, dried distillers grains with soluble (DDGS) and other fodder such as straw, silage and finished feed [7].

From the 804 survey samples analysed, 31 %, 48 %, 62 %, 63 % and 32 % tested positive for contamination with Afla, ZON, DON, FUM and OTA, respectively.

Mycotoxins are a ubiquitous problem as 89 % of the analysed samples show the presence of, at least, one mycotoxin (fig. 1).

The presence of more than one mycotoxin in 53 % of the samples raises the attention to the problem of synergistic effects caused by multiple mycotoxins in animal feeds [7].



Source: www.biomin.com

Figure 1. Overview on the distribution of mycotoxins amongst different world regions (% refers to percentage of positive samples - >LOD -)

3. Conclusions

Fusarium species produce an extraordinary diversity of biologically active secondary metabolites, some of which are harmful to animals and, thus, mycotoxins. Trichothecenes, zearalenone and fumonisins are distributed widely in cereal crops, to the extent of ubiquity in certain crops grown in specific regions and seasons. Most economic losses due to the consumption of mycotoxin-contaminated diets by farm animals result from reduced animal production and increased disease incidence.

Animal diseases such as infertility, vaginal or rectal prolapse, anorexia, skin and gastrointestinal irritation, haemorrhaging, abnormal offsprings, pulmonary edema, liver tumours, etc. could be ascribed to the consumption of feed contaminated with these mycotoxins.

Finally, it is suggested that the long-term objective should be to reduce natural contamination

of cereal grains and forages through the exploitation of disease-resistant cultivars.

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