Six Detrimental Effects of Mycotoxins on the Gastrointestinal Health of Poultry

PEER REVIEWED

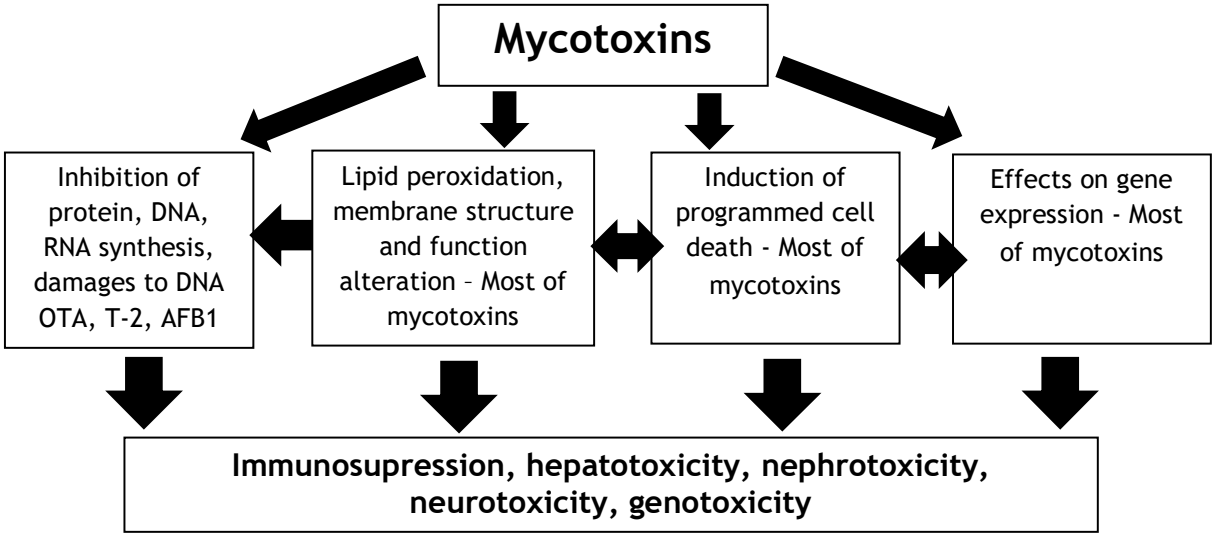
Contamination of feed commodities by moulds and mycotoxins is considered to be one of the most important negative factors in crop production and animal feed quality.

It is well documented that mycotoxin consumption causes a decrease in performance as well as decreased growth rate and poor feed efficiency (Pestka, 2007; Hanif *et al.*, 2008). The most important source of mycotoxins is feed. It is known that 95% of all mycotoxins come from the field. More than 300 mycotoxins have been shown to induce signs of toxicity in mammals and avian species, and this number is increasing. It has been estimated that 25% of the world's crop production is contaminated with mycotoxins (Surai and Mezes, 2005). The most significant mycotoxins in naturally-contaminated foods and feeds are aflatoxins (Afla), ochratoxin A (OTA), zearalenone (ZEN), T-2 toxin, deoxynivalenol (DON) and fumonisins (FUM). In many cases, these mycotoxins can be found in combination in contaminated feed. The effects of the most economically important mycotoxins in different poultry categories (broilers, layers and breeders) are usually: reduction in feed consumption and weight gain, decreased resistance to pathogens - immunosuppression, reduced egg production and hatchability, decreased semen volume and testes weights, fatty livers and enlarged spleens, rickets, leg weakness, impaired shell quality and different kinds of lesions (oral, skin, kidney, liver and gizzard). Major mechanisms of mycotoxin toxicity are described in picture 1. There has been extensive research addressing the different ways in which mycotoxins can alter animal productivity. In this article, the emphasis is on six major effects of mycotoxins in the intestine that may contribute to decreased performance. In addition, the possible alteration of the microflora by mycotoxins will be explored.

1. Mycotoxins affect the intestinal mucosa

The gastrointestinal tract represents the first barrier against ingested chemicals, feed contaminants, and natural toxins. Following ingestion of mycotoxin-contaminated feed, intestinal epithelial cells can be exposed to high concentrations of toxins. This is especially important when considering toxins that have poor intestinal absorption, such as fumonisin B1 (Bouhet *et al.*, 2004). Direct intestinal damage can be caused by the biological actions of mycotoxins. Trichothecenes affect actively dividing cells, such as those lining the gastrointestinal tract. There are direct effects of trichothecenes on protein synthesis in eukaryotic cells due to the interaction with the ribosomal units, preventing either initiation of protein synthesis or elongation of the polypeptidic chains (Ueno, 1984). It should be noted that the gastrointestinal tract is also sensitive to trichothecene-induced apoptosis, affecting mainly the gastric mucosa, gastric granular epithelium, and intestinal crypt cell epithelium (Bondy and Pestka, 2000). The toxic action of trichothecenes results in extensive necrosis of oral mucosa and gizzard lesions (Leeson *et al.*, 1995). The T-2 toxin inhibits DNA, RNA, and protein synthesis in eukaryotic cells, affecting the cell cycle and inducing apoptosis both *in vivo* and *in vitro* (Rocha *et al.*, 2005). It should also be mentioned that the primary effect of T-2 toxin is executed by its contact with the mouth epithelium (beak cavity and tongue).

Another important effect of some mycotoxins, such as fumonisin B1 and ochratoxin A, is that they alter the barrier function of the intestinal epithelium, which is measured as a decrease in the transepithelial electrical resistance. It is likely that the environment surrounding the tight junctions



Picture 1: Major Mechanism of mycotoxin toxicity (Adapted from Suraj and Dvorska, 2005

is somehow altered by continuous exposure to fumonisin B1 (Bouhet *et al.*, 2004; McLaughlin *et al.*, 2004). Poults fed grains naturally contaminated with fusarium mycotoxins had decreased villus height in the duodenum, and decreased villus height and villus surface in the jejunum during the starter period. In turkeys fed the same diet contaminated with fusarium mycotoxins, the width and villus surface of the duodenum, villus height and surface of jejunum, and submucosal thickness of ileum were decreased during the grower phase (Girish and Smith, 2008). Broilers fed diets contaminated with 0.5 mg deoxynivalenol/kg had shorter and thinner villi, which resulted in lighter small intestines compared to birds fed control diets (Awad *et al.,* 2006).

2. Mycotoxins affect intestinal secretions
Aflatoxins fed to broiler chickens decreased the production of pancreatic secretions, whereas aflatoxins fed to layers produced an increase in the production of pancreatic enzymes (Osborne and Hamilton, 1981; Richardson and Hamilton, 1987). Intestinal morphology (intestinal crypt depth) and the specific activity of intestinal disaccharidase and maltase were also altered by feeding aflatoxin B1 (AFB1) (Applegate *et al*., 2009).

3. Mycotoxins affect intestinal nutrient absorption
In addition to the morphological changes induced to the intestinal villi by DON, it is suggested that this mycotoxin inhibits Na+ transport and Na+-D-glucose co-transport in the jejunum of layers. This results in a reduction of glucose uptake when the intestine is exposed to DON concentrations of 10 mg /L (Awad *et al*., 2005a; 2007). Similarly, in layers, DON affects the intestinal absorption of the amino acids that are co-transported with sodium, such as L-Proline (Awad *et al.*, 2005b).

4. Mycotoxins and intestinal microflora
Direct microbial toxicity of several mycotoxins has already been reported. *E. coli*, and *S. aureus* are susceptible to AfB1. This toxin inhibits the growth of these bacteria by up to 60%, depending on the bacterial strain. Bacteria that are more resistant to antibiotics have a tendency to be more resistant to the effect of mycotoxins (Tiwari *et al.*, 1986). *B. brevis, B. cereus, B. megaterium, B. subtilis, B. thuringiensis, B. pumilus* and *Listeria ivanovii* are also sensitive to several mycotoxins (Madhyastha *et al*., 1993). *Streptomyces vinaceous, S. olivoreticuli, S. lavendulae, S. roseochromogenes, S. virginiae, Nocardia leishmanii* and *N. coelica* were also inhibited to certain degrees by aflatoxins, at concentrations ranging from 10 to 100 µg/mL (Tadashi *et al.,* 1967). In addition to the direct toxic effects of mycotoxins on bacteria, there may be additional indirect effects. There is reported communication between the intestinal cells and microflora. If the capability of epithelial cells to synthesise proteins is reduced, a change in the signals that the enterocytes are transmitting to the microflora may be hypothesised.

5. Pathogen colonisation is enhanced by mycotoxins
Although some bacterial strains are affected by mycotoxins, there is evidence that mycotoxins increase pathogenic bacterial colonisation of the intestinal tract in poultry and other animal species. Similarly, layer chickens treated with 3mg/kg of ochratoxin A had higher susceptibility to a Salmonella challenge compared to the control group (Fukata *et al.,* 1996). *E. coli* challenge in broilers receiving an experimental diet containing 2 ppm of ochratoxin more than doubled the mortality compared to birds that received the bacterial challenge and a diet without mycotoxins. No birds died in the group that received the mycotoxin alone diet, demonstrating that it is the combination of mycotoxins and pathogenic bacteria that causes the most devastating effects (Kumar *et al.,* 2003). Gross and histopathological lesions of birds inoculated with E. coli were also more severe in birds that received a diet containing 2 ppm of ochratoxin than in birds that received a diet with no significant levels of mycotoxins (Kumar *et al.*, 2004). Parasitic infections are more severe in combination with mycotoxins. It has been demonstrated that birds treated with lasalocid developed clinical coccidiosis when the levels of T-fusariotoxin exceeded 0.5 ppm (Varga and Ványi, 1992).

6. Mycotoxins alter intestinal motility
Subchronic ingestion of DON, comparable with concentrations occurring in contaminated food and feed, was reported to impair the intestinal transfer and uptake of nutrients. Black sticky diarrhoea was reported in a flock of 6700 laying hens in India after the consumption of a feed batch contaminated with fumonisin B^1 (6.5 mg/kg feed) and aflatoxin B1 (0.1 mg/kg). Haemorrhages of the proventriculus and accumulation of fluid in the intestine were commonly seen in the postmortem examinations. The disease was then experimentally reproduced in day-old chicks and in laying hens by feeding the contaminated diet (Prathapkumar *et al*., 1997).

By combining the different areas covered in this article, it becomes clear that the intestinal microflora could be affected by mycotoxin ingestion via the following ways:

1) **Mycotoxins affect the intestinal mucosa:** Necrotic tissue released into the lumen changes the local environment. Receptor sites are lost and inflammatory cells get to the injured site and secrete toxic metabolites. In addition, mucus production is increased, changing the quality of nutrients available in the lumen.

2) **Mycotoxins affect intestinal secretions:** This generates a change in the chemistry of the luminal environment. The bacteria that are most suitable to the new luminal environment will have more chances of successfully multiplying.

3) **Mycotoxins affect nutrient absorption in the intestine:** The quality and quantity of nutrients available in the intestinal lumen changes since absorption capacity is altered. It is likely that species of bacteria that can successfully ferment the new "luminal diet" will predominate in the lumen.

4) **Bacteria are affected by mycotoxins:** It is reported that several genera of bacteria are sensitive to at least one mycotoxin. Species of bacteria that are more resistant to the mycotoxins will probably replicate at an increased rate, changing the ecosystem of the microflora.

5) **Pathogen colonisation is enhanced by mycotoxins:** This is probably a consequence of a weakened immune system plus altered microbial ecosystem (dysbiosis).

6) **Mycotoxins alter intestinal motility:** The quality and quantity of nutrients available for fermentation in a determined location are dependent on the flow rate, thus the bacterial population will readapt to the new environment. In addition, increased motility will physically eliminate the bacteria that have their niche closer to the tips of the villi, compared to those that find a more favourable environment towards the bottom of the villi (villi probably serve as a mechanical barrier). For bacteria that live predominantly close to the top section of the villi, a rapid reproduction rate will give them higher chances of survival under increased transit rate.

Mycotoxin Management

Although agronomic and other practices are aimed at decreasing or eliminating mycotoxins in the field, there are still considerable reasons to look at post-harvest ways to counteract mycotoxins in grains and other commodities. Costs and limitations of physical and chemical treatments prompted the search for other solutions concerning the mycotoxin hazard.

The best practical way to control mycotoxin levels is to use rapid test kit systems for the analysis of mycotoxins in raw ingredients which are not yet in silos. Different rapid test kit systems are validated for different mycotoxins and commodities offering a very quick and effective way of raw material screening before they enter the feed mill. Once the levels are known, every feed mill can estimate the quality of its raw ingredients in terms of mycotoxin contamination and can effectively and more precisely (by dosage adjustment) apply feed additives during feed production.

Another strategy of mycotoxin risk management is to test for the presence of mycotoxins in finished feeds including total mixed ration (TMR) and silages. This method has some advantages and disadvantages. Since each raw ingredient can bring its own mycotoxins into the finished feed, the most important advantage is that the presence of raw ingredients with a low inclusion rate (5-10%) – which can still cause significant contamination of the finished feed but can be inadvertently overlooked if not tested - can be identified by testing the finished feed. The most important disadvantage is that analysis of finished feed takes quite a long time, such that the tested feed is likely to have been fed to the animals by the time the results from the analysis are known. Storage mycotoxin contamination (ochratoxins, aflatoxins) can be prevented by keeping temperature and moisture content in silos low, whilst aerating the grain regularly. In cases where perfect storage conditions cannot be guaranteed, the use of mould inhibitors and silage inoculants is highly recommended. The application of specific feed additives (mycotoxin deactivators) which are able to help reduce the negative effects of different mycotoxins in dairy cows is highly recommended.

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