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A REVIEW OF THE IMPACT OF MYCOTOXIN CONTAMINATION ON POULTRY PERFORMANCES

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ABSTRACT

Extensive research over several decades has revealed that mycotoxin is commonly found in most poultry feed ingredients. All poultry is sensitive to mycotoxins. This partly depends on the type, age, and production categories of poultry, their living conditions, and nutritive status and partly on the type, quantity, and duration of mycotoxin ingestion. Mycotoxins are toxin secondary metabolites produced primarily by fungi of the genera Aspergillus, Fusarium, and Penicillium that have harmed poultry, animal, and human health for thousands of years. Some common effects of mycotoxin are reduced feed intake, weight gain, feed efficiency, growth performance, immunity and hatchability along with increased mortality, organ damages (mainly kidney and liver), carcinogenicity, teratogenicity and decreased egg production. There is a strong need to evaluate the effect of mycotoxin on poultry performances and their importance.

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1. INTRODUCTION

The term "mycotoxin" is derived from the greek word "mykes" meaning fungus and "toxicon" meaning poison. Mycotoxin are a secondary metabolite produced by fungi that is capable of causing disease and death in both humans and animals. Mycotoxin occurrence is a significant global challenge, accompanied by rising animal and human health risks and massive financial losses in the food and feed production industries (Pinotti *et al*., 2016). In addition to the usual stressors associated with intensive rearing practices, poultry can be vulnerable to a wide range of mycotoxins. Under aerobic conditions, fungal growth occurs in a variety of feed raw materials. Mycotoxins are produced by approximately 200 species of fungi. The majority of the fungi that form mycotoxin belongs to three geniuses: Aspergillus, Penicillium and Fusarium. Aflatoxins (AF), zearalenone (ZEN), ochratoxin A (OTA), fumonisins (FUM), trichothecenes such as deoxynivalenol (DON), and T-2 toxin are some of the mycotoxins that can significantly impact the health and productivity of poultry species. Fungal growth and mycotoxin production initiate in the cropland, during transportation or storage, and

are affected by the environmental conditions including seasons, location of grain cultivation, drought and time of harvest. Long-term analyses show that feed and feedstuffs may be contaminated with mycotoxins, where these contaminated feed materials often include more than one mycotoxin (Streit *et al*., 2013a).

Mycotoxins affect 25% of the world's growing crops each year, resulting in annual losses of about 1 billion metric tons of food and food products, according to a report by the Food and Agriculture Organization (Manafi *et al.,*2014). Acute cases caused by high levels of mycotoxins in the diet can result in mortality and a significant decrease in poultry productivity, as shown by clinical signs and post-mortem lesions. The extra cost involves the management of mycotoxin, such as prevention, control, sampling, mitigation, labor loss and research costs. some others effect are their undesirable health effects, decrease in the production rate due to the spoilage of feed, and overall economic effects which are reflected in international trade of food and food products. Therefore, control of the fungal development and mycotoxin production are crucial for feed and animal producers. Mycotoxins are metabolized in the alimentary canal, liver, or kidneys of the poultry in accordance with their chemical properties. Their transfer to poultry meat and eggs leads to unpleasant health effects in humans, leading to major concerns in public health. Contamination of the feeds with fungi damages both their organoleptic properties and increases poisoning risk by decreasing their nutritional value. Toxicity of the mycotoxins depends on the amount of absorption, number of the metabolites that are formed, exposure period, and sensitivity of the animal.

The recognition that mycotoxins affect the health and productivity of poultry has led to intensive research on counteracting methods over the last few decades, including detection and elimination or detoxification of mycotoxins. Although enzyme-linked immunosorbent assay (ELISA) based detection methods were used in the past, recent developments in the analysis and detection of mycotoxins in feed and feed ingredients improved the scenario considerably. The use of high performance liquid chromatography (HPLC) has been one such development which initiated the path to detect multiple mycotoxins simultaneously in a sample (Schumacher *et al*., 1997). The latest technique using liquid chromatography coupled to (tandem) mass spectrometry (LC-MS/MS) increased this potential phenomenally to detect hundreds of mycotoxins simultaneously in a sample (Malachova *et al*., 2014). This new development has also led to the detection of masked and emerging mycotoxins, which are neither routinely screened nor regulated by legislations (Berthiller *et al*., 2013).

The objective of this review is to discuss in detail the effect of mycotoxin on poultry performances and their important, along with recent development in the strategies to prevent mycotoxins.

2.0 MYCOTOXINS IN POULTRY PRODUCTION

2.1 AFLATOXINS

Aflatoxins are poisonous carcinogen and mutagens that are produced by certain Aspergillus fungi, such as *A. flavus* and *A. parasiticus*. They are often found in feed ingredients used for poultry rations example; Aflatoxins B1 (AFB1), G1 (AFG1) and their dihydroxy derivatives B2 (AFB2) and G2 (AFG2) naturally contaminated feeds. Aflatoxin M1 and M2 (AFM1 and AFM2), the 4-hydroxy metabolites of AFB1 and B2 presence in biological fluids including milk and tissues, is related to the exposure of the contaminated feed (Dohnal *et al*., 2014). AFB1 was identified in the early 1960s as the main etiological agent of "Turkey X Disease" responsible for the death of young turkeys in England as a result of contaminated

peanut-based feed (Rawal *et al*., 2010). It is a major public health concern globally, and it is a widespread dietary hepatotoxin and hepatocarcinogen.

AFB1 is a "pro-carcinogen" that is activated to a reactive form by the enzyme hepatic microsomal cytochrome P450 (CYP450), whereas electrophilic AFB1-8,9-epoxide (AFBO) is required for carcinogenic and toxic activity. Among the known AF, AFB1 is most encountered and considered the most toxic classified as a human carcinogen (Yunus *et al*., 2011). Major metabolites of AFB1 formed in chicken liver are AFM1 and AFB2a. AFB1 and B2 are then degraded to cyclopentanol and aflatoxicol through NADP. Both AFB1 and aflatoxicol are known to accumulate at the layer of the egg. While AFB1 and AFM1 are present in chicken muscle and blood, the levels are found much higher in turkeys; the aflatoxicol levels were found to be less prominent in these animals. As a comparison, 1/1200 of AFB1 taken with feeds was found to accumulate in poultry meats, while 1/2200 of AFB1 was found to accumulate in the eggs (Hossain *et al*., 2011).

Effect of Aflatoxin in poultry includes weight loss, poor feed efficiency, losses in egg production and egg weight, increased liver fat, changes in organ weights, reduction in serum protein levels, carcass bruising, poor pigmentation, liver damage, decreased activities of several enzymes involved in the digestion of starch, protein, lipids, and nucleic acids, and immunosuppression (Murthy *et al*., 2005). Evidence suggests that immunosuppression caused by AF results in many disease outbreaks, vaccination failures, and poor antibody titers. At necropsy, livers are usually pale and enlarged, as a result of aflatoxicosis. Ingestion of 2 ppm AFB1 in male broiler chicks was found to cause upregulation of several hepatic genes. For example, enzymes involved in energy production and fatty acid metabolism (carnitine palmitoyl transferase), development and growth (insulin-like growth factor 1), coagulation (coagulation factors IX and X), immune system defense (interleukins), and antioxidants protection (GST), detoxification (epoxide hydrolase) were found to be downregulated; while cell-proliferation enzymes (ornithine decarboxylase) were upregulated (Yarru *et al*., 2009).

2.2 OCHRATOXINS

Ochratoxin is a toxin found in agricultural products all over the world. The term "Ochratoxin" was derived from the name of the mould: Aspergillus ochraceous from which the ochratoxins were first isolated. Ochratoxins are produced by several species of *Aspergillus (Aspergillus ochraceous*) and *Penicillium (Penicillium verrucosum*). *Aspergillus ochraceous* produces OTA in hot climates (troical regions), while *Penicillium verrucosum* produces it in temperate climate can grow when the temperature is as low as 5 ºC. Ochratoxin are groups of fungal metabolite that consists of three types, A, B and C. Ochratoxin A (OTA) is the most prevalent and the most toxic. It is considered as a secondary toxic metabolite produced mainly by some strains of fungi such as *Aspergillus ochraceus*. ochratoxin are produced at moderate temperatures with high water activity and it Preferably grow in oilseeds (peanuts and soybeans) more than in grain crops, such as wheat and corn and *Penicillium verrucosum* species which grows at cool temperate regions (5-30°C) with law water activity, thus produce ochratoxin in wheat and corn. Also, nutritional, humidity, water activity and integrity of the seeds are factors that influence on mold growth and produce ochratoxin. Different carbon sources, including glucose, sucrose, lactose or xylose, appear to repress OTA production in *A. ochraceus*; other compounds, such as lactose, and organic nitrogen, such as urea and amino acids, influence its production.

Ochratoxins are derived from isocoumarin and L-b-phenylalanine, and are classified as pentapeptides. OTA is primarily a nephrotoxin, the nephrotoxic effect of OTA has been shown in many animal species, mostly sensitivity is variable among them (Abarca *et al*., 2001). OTA also has teratogenic, immunosuppressive, carcinogenic, and hepatotoxic effects. Poultry is less sensitive to OTA, due to their higher capacity of excreting OTA compared to other species. Several experiments reported negative effects of OTA feed contamination on poultry performances.

The high weight found in the liver and kidneys, organs involved in the detoxification and removal of OTA from the blood, maybe due to either of these metabolic disorders. Some lymphoid glands, such as the thymus, Fabricius' bursa, and the spleen, however, displayed degeneration and decreased weight as a result of the decreased number of antibody-producing cells (Stoev *et al*., 2012) observed macroscopical, histopathological, hematological, and biochemical changes in chicks fed an OTA-contaminated diet for six and ten weeks. The blood levels of chicks indicated an alteration of hematopoiesis, which was characterized by mild anemia. Furthermore, higher serum levels of uric acid, urea, and creatinine, as well as lower levels of serum total protein and high urinary protein excretion, were observed, suggesting potential serious kidney damagells.

In a necropsy analysis of chickens fed a diet containing OTA at 2 mg/kg for three and four weeks (Santin *et al*., 2010) found alterations in internal organs such as pale swollen kidneys and enlarged, yellowish and friable at palpation livers. In addition, histopathological examinations showed vacuolation and megalocytosis of hepatocytes, hyperplasia of the biliary epithelium and hypertrophy of renal proximal tubular epithelial cells. In broiler chicks fed a diet with 2 mg/kg of OTA, no changes were observed within the first three weeks of treatment. However, after five weeks, remarkable changes in organs such as swelling of kidneys, slight enlargement of liver and reduction in size of the bursa of Fabricius. Moreover, histopathological analyses showed marked changes in the lesion score of organs, which was the highest for kidneys followed by the liver, bursa, spleen and thymus. Kumar *et al* confirmed that OTA is more a nephrotoxin than a hepatotoxin for broilers: most relevant effects observed on animals fed a diet contaminated with OTA at 2 mg/kg were atrophy of the bursa, thymus and spleen along with the depletion of lymphocytes. In a recent study carried out on two commercial poultry farms, Bozzo *et al*. detected OTA in all feed samples, with a concentration ranging between 0.160 and 0.332 mg/kg. The OTA contaminated feed was administered to animals for at least two months. Postmortem inspection and the cytological and histological examinations of the layer hens evidenced gross and microscopical lesions in the kidneys and liver. Sawale *et al* reported negative effects of OTA on performance, hematobiochemical disturbances and severe immunosuppression in laying hens fed a diet contaminated with OTA at 1mg/kg of feed for 60 days.

In a study, oral LD50 values were reported for OTC (216 mg animal-1) and OTA (166 mg animal-1) in day-old chicks. Other ochratoxin ethyl or methyl esters showed lower toxicity compared to OTA. In comparison to OTA, the methyl ester of OTA was less toxic than OTA in day-old chicks, while OTB methyl and ethyl esters were found to be non-lethal to orally exposed day-old ducklings (Heussner *et al*., 2015).

2.3 FUMONISINS

Fumonisins (FUM) are a class of mycotoxins first isolated from *Fusarium moniliforme* cultures and chemically characterized by Gelderblom and colleagues in 1988. Six separate FUMs (A1, A2, B1, B2,

B3, B4) have been identified and their structures deduced. Fumonisin B1 (FB1), on the other hand, has been reported to be the most common form developed by *Fusarium moniliforme*. Several other Fusarium species, as well as a species of *Alternaria*, have been discovered to produce FB1. Based on all of these animal tests, the International Agency for Research on Cancer has identified FB1 as potentially carcinogenic to humans (Group2B). *Fusarium verticillioides*, on the other hand, have been reported to produce fumonisin B1 (FB1) as the most common type (Domijan *et al*., 2012).

Chicks and turkeys, two susceptible species, are relatively resistant to the toxic effects of FB1. Mild to moderate toxicity was observed in chicks, ducks, and turkeys fed 75—400 mg FB1/kg for 21 days. In chicks, ducks, and turkeys, the primary changes were decreased body weight gain and liver pathology. In chicks, hepatic changes included multifocal hepatic necrosis and biliary hyperplasia. One study also found hepatocellular hyperplasia and increased extra medullary hematopoiesis. In turkeys fed 150—300 mg FB1/kg and ducklings fed 400 mg FB1/kg, the primary liver pathology observed was diffuse hepatocellular hyperplasia with biliary hyperplasia (more evident in turkeys). In studies designed to assess the long-term effects of FB1, up to 50 mg FB1/kg diet had no effect on chick performance up to 7 weeks, whereas turkeys fed 50 mg FB1/kg diet had lower feed intakes than birds fed 0 or 25 mg FB1/kg diet (Broomhead *et al*., 2002).

The disruption of sphingolipid metabolism appears to be the mechanism causing fumonisin toxicity in animals. According to current evidence, FUM are specific inhibitors of ceramide synthase (sphinganine/sphingosine N-acyltransferase), a key enzyme required for the synthesis of ceramide and more complex sphingolipids. When this enzyme system is inhibited, tissue concentrations of the sphingolipids sphingosine (SO) and sphinganine (SA) rise, as does the SA:SO ratio. The SA:SO ratio was found to be higher in tissues from broilers, turkeys, and ducklings fed FB1 (Tran *et al*., 2005).

2.4 TRICHOTHECENES

Trichothecene mycotoxins are a class of fungal metabolites that share the same basic backbone structure. They include T2 toxin, HT2 toxin, diacetoxyscirpenol (DAS), monoacetoxyscirpenol (MAS), neosolaniol, 8-acetoxyneosolaniol, 4-deacetylneosolaniol, nivalenol, 4-acetoxynivalenol (Fusarenone-X), DON (vomitoxin) and 3-acetyldeoxynivalenol (Leeson *et al*., 1995). Trichothecenes are the most potent small-molecule inhibitors of protein synthesis known, with a primary inhibition of protein synthesis accompanied by a secondary disruption of DNA and RNA synthesis as the key toxic effect at the cellular level (Murugesan *et al*., 2015) DON, a common contaminant of corn, wheat, and other commodity grains, is the most effective trichothecene mycotoxin for livestock. T2 toxin and DAS are present in smaller concentrations sporadically in the same sources. Pigs are more sensitive to trichothecenes than poultry and cattle. T2 toxin is less common in crops than the associated DON toxin. According to some studies, trichothecenes like DON, nivalenol, and fusarenon X are more common (57 percent, 16 percent, and 10% of tested grain samples) in European grain samples than trichothecenes like T2 toxin (20 percent), HT2 toxin (14 percent), T2 tetraol (6 percent), neosolaniol (1 percent), DAS (4 percent), and MAS (1 percent) (Sokolovij *et al*., 2008).

Oral lesions, growth retardation, abnormal feathering, reduced egg development and egg shell consistency, regression of the Fabricius bursa, peroxidative changes in the liver, abnormal blood coagulation, leucopoenia and proteinemia, and immunosuppression are all toxic effects of trichothecenes. Trichothecene poisoning can

be acute or chronic in poultry. Acute poisoning has a distinct clinical image and is easily detected, whereas chronic poisoning has a wide range of symptoms (Resanovic *et al*., 2009). T2 concentrations that induce oral lesions are lower (0.4 mg/kg) than those that have been shown to reduce chick output (3—4 mg/kg) (Murugesan *et al*., 2015). Danicke concluded in a systematic analysis that broiler performance is harmed at dietary concentrations of 3—4 mg/kg of T2 toxin, while duck performance is harmed at dietary concentrations as low as 0.4 mg/kg.

During *Mycoplasma gallisepticum* infections in broilers, T2 toxin can cause a decrease in body weight and relative weights of the bursa of Fabricius, thymus, and spleen, swollen liver, friable, and yellowish discoloration with distended gall bladder, as well as a decrease in body weight and relative weights of the bursa of Fabricius, thymus, and spleen. In the bile duct epithelia, microscopical findings include vacuolar degeneration and augmented hyperplasia; Kupffer cell activity and infiltration of inflammatory cells in the liver; vacuolar degeneration with pyknotic nuclei in the kidney; lymphocytolysis and reduction of prominent reticuloepithelial cells in lymphoid organs; desquamation of villous-type epithelial cells and lymphoid intrusion in the submucosa of proventriculus; mild hemorrhage along with inflammatory cells in the heart; desquamation and erosion of the mucosa in trachea and the thickening of the air sacs along with edema and the presence of inflammatory cells in air sac (Manafi *et al*., 2015)

Deoxynivalenol is less toxic than T-2 toxin, though the amount of DON that affects chick output is still up for discussion, with some researchers reporting toxic effects at 16 mg/kg diet, while others (Moran *et al*., 1982) reporting no toxic effect before dietary concentrations of DON exceeded 116 mg/kg. Danicke *et al*., (2001) reviewed the findings of 49 DON studies and concluded that a dietary concentration of 5 mg/kg had no adverse effects on results. In poultry, deoxynivalenol has been shown to have both immunosuppressive and immunomodulatory effects. DON, at concentrations ranging from 1 to 7 mg/kg diet, has been shown to dramatically alter many main functions of the intestinal tract, including decreasing villus surface area available for absorption and altering intestinal permeability (Awad *et al*., 2011; Osselaere *et al*., 2013).

2.5 OTHERS TYPE OF MYCOTOXIN THAT AFFECT POULTRY

2.5.1 ZEARALENON

Poultry is very resistant to zearalenon. Of all species of poultry, turkey is the most sensitive to the effects of zearalenon, which can cause a decrease in their egg-laying ability even up to 20% (Allen *et al*., 1983). The immunosuppressive effects of zearalenon in poultry have not been proved so far.

2.5.2 CYCLOPIAZONIC

Cyclopiazonic acid is not a common contaminator of food and poultry feed. However, when detected, cyclopiazonic acid can, depending on the quantity and duration of ingestion, cause a very dramatic clinical picture of the central nervous system disorder manifesting itself as ataxia, paresis, paralysis, and opisthotonus. Prominent cumulative toxicity of cyclopiazonic acid can be observed. A decrease in the weight of bursa Fabricii followed by an incerease in the weight of liver, kidneys, and forestomach can also be detected. The decrease in the weight of bursa Fabricii leads to a weakened immune response after vaccination.

3.0 EFFECT OF MYCOTOXIN ON POULTRY PERFORMANCES

Mycotoxins have a large economic and commercial effect because they reduce the productivity and nutritional value of contaminated cereals and forages (Ratcliff, 2002). The effect of mold contamination on the nutritional value of stored maize is shown in Table 1. The nutritional value of stored

maize decreases after mold contamination. Since mycotoxins reduce the production and nutritional value of infected cereals and forages, they have a significant economic and commercial effect (Ratcliff, 2002). The nutritional value of stored maize is shown to be impaired by mold contamination. The nutritional value of stored maize decreases as a result of mold contamination, depending on the volume consumed, the number of toxins present, duration of exposure to mycotoxins and animal sensitivity.

Table 1: Effect of mould contamination on natural value of stored maize

	ME (Kcal/kg)	CP (%)	Fat (%)
Good corn	3,410	8.9	4.0
Mouldy corn	3,252	8.3	1.5
Loss in nutrient	158	0.6	7.5
% Loss in nutrient	4.6	6.7	62.5

ME = Metabolisable energy. CP = Crude protein

Source: Okeeffe (2003).

Mycotoxins can also cause health issues that are unique to each toxin, as seen in Table 2, or impair an animal's immune status, making them more susceptible to infections. This is one of the key reasons why diagnosing mycotoxicoses is so complicated (Yiannikouris and Jonany, 2002). In species, mycotoxins have a wide variety of negative consequences. Reduced animal productivity, increased disease occurs due to immunosuppression, damage to vital organs and conflict with reproductive capability have much greater economic consequences than death from mycotoxin poisoning. In contrast to their individual effects, mycotoxins in combination tend to have a greater negative impact on livestock health and productivity (Smith and Seddon, 1998).

Table 2: Mycotoxins and their effects on poultry.

Mycotoxins	Species susceptibility	Effects
Aflatoxin	All domestic animals and poultry	Hepatoxic, carcinogenic, immunosuppressive
Ochratoxin	Mainly pigs and poultry	Nephrotoxic, gout
Fumonisins	Mainly pigs and horses	Neurological disorders, liver damage.
T-2 toxin	Mainly pigs and poultry	Mouth lesions, loss of appetite

Source: Ratcliff (2002).

3.1 INTERACTIONS AMONG MYCOTOXINS

In nature, co-occurrence of mycotoxins is generally observed. A single fungus can produce a variety of mycotoxins, and many species can produce the same mycotoxin. A meta-analysis of over 100 publications documenting toxicological interactions among mycotoxins was published in a paper. Most of

the experiments revealed a synergistic or additive effect on animal results, according to the findings. However, results for other response variables revealed a variety of interactions ranging from synergistic to antagonistic for the same association (Grenier*et al*., 2011). They also discovered in their review that a combination of mycotoxins, even at concentrations that should not have a negative effect on animals, can have a negative effect on them.

From 8 to 41 days of age, the effects of dietary AFB1 and FB1 on liver pathology, serum levels of aspartate aminotransferase (AST), and plasma total protein (TP) of broilers were measured using AFB1 (0, 50, and 200 g AFB1/kg) and FB1 (0, 50, and 200 mg FB1/kg). At 6 days after feeding, TP levels were found to be lower in the AFB1treated group (200 g) and the FB1 combination group. The combination group (200 g AFB1 and 200 mg FB1) was found to have higher plasma TP, proliferation of bile duct and trabecular disorders in liver tissue compared to controls at 33 days' post feeding, while the changes in the other groups were insignificant compared to controls (Tessari *et al*., 2010). Aflatoxicosis causes laying hens to produce fewer eggs and have lower egg weights. Meanwhile, the antagonistic effects of AF and FB on egg production in quails have been reported, with a significant decrease in egg production in the FBonly treated group compared to the AF+FB combination (Ogido *et al*., 2004).

The combined effect of AF and FB on immunity has only been studied in a few studies. As AF and FB co-contaminated feed was compared to single contamination, it was discovered that co-contamination reduced lymphocyte proliferation by mitogenic stimulation by less than or equal to additive. Antibody titers against Newcastle disease were found to decrease synergistically in a sample (Tessari *et al*., 2010; Harvey *et al*., 1995). When looking at the hemagglutination titers against sheep red blood cells in turkey poults, another study found an unusual increase and additive effect of the two toxins. Dietary treatment did not affect the phytohemagglutinin delayed hypersensitivity response. These findings suggest that FB1 and AF, both alone and in combination, may have a negative impact on poult performance and health.

In chickens, AF and OTA infected feed caused microscopic lesions in the liver and kidneys, as well as their respective target organs, despite conflicting findings in different studies. As a result, OTA in the diet was discovered to prevent AF-induced hepatic fatty infiltration in chickens. On the contrary, a study found that chickens fed the cocontaminated diet had more serious hepatic lesions, including granular and vacuolar degeneration, necrosis of the liver parenchyma, and hemorrhage regions (Sakhare *et al*., 2007). Renal injuries occurred earlier and were more developed in chickens fed a multicontaminated diet than in animals fed a monocontaminated diet, according to a report, which resulted in tubular epithelium degradation and tubular cell detachment from the basement membrane (Sakhare *et al*., 2007). These disputes may be explained by the species used. Aside from that, chronic DON exposure had no effect on FB1 toxicokinetics in broilers (Antonissen *et al*., 2015).

The data on combination toxicity is still limited and occasionally contradictory. Mycotoxin interactions are currently unknown, even though combined exposure is more relevant to real-life conditions. It is well known that the combined effects of mycotoxins are mostly additive or synergistic; however, depending on the concentrations and in vitro model used, antagonistic effects can occur (Heussner *et al*., 2015).

Table 3. Impact of co-contamination by mycotoxins in poultry

Mycotoxins	Species tested	Production effects	References
Aflatoxin & Diacetoxyscripenol	Broiler chicks	Synergism	Kubena *et al*., 1993
Aflatoxin & T-2 toxin	Broiler chicks	Synergism	Aravind *et al*., 2003; Girish *et al*., 2004
Aflatoxin & Ochratoxin	Broiler chicks	Synergism	Kubena *et al*., 1989; Raju & Devegowda, 2000
Ochratoxin & T-2 toxin	Broiler chicks	Synergism	Raju & Devegowada,2000
Deoxynivalenol & Fusaric acid	Broiler chicks	Synergism	Smith *et al*., 2000; Swamy *et al*., 2002

4.0 PREVENTION AND CONTROL

Fungi production in feeds can be avoided by keeping feeds fresh, keeping humidity low, and keeping equipment clean, as well as adding fungistatic substances. Humidity levels above 11% encourage fungal growth in cereals and feed. High relative humidity storage conditions have a direct effect on the feeds humidity quality. The feed and storehouse raw materials are dehumidified by good storehouse ventilation. Physically damaged cereals are more susceptible to fungus development than healthy cereals. Changing raw materials at storage locations at regular intervals reduces the formation of mycotoxin (Demircioglu *et al*., 2010; Kaya *et al*., 2014).

Monitoring and good agricultural, storage, and transportation practices, as well as an efficient Hazard Analysis and Critical Control Point (HACCP) strategy, do not, however, fully eliminate mycotoxin contamination in the food and feed chain. Decontamination techniques are then used as a last resort to save polluted batches in the manufacturing process. Given the diversity of mycotoxin structures, it is reasonable to conclude that there is no single method for deactivating mycotoxins in feed. As a result, various methods must be combined to target individual mycotoxins while preserving feed consistency (Bhat *et al*., 2010)

Different methods are used to decontaminate mycotoxin-contaminated commodities or to minimize mycotoxin exposure, but not all of them are suitable for feed and compound feed producers. A good approach for reducing mycotoxins should be able to inactivate them without leaving toxic residues or compromising the product's technical properties or palatability (Murugesan *et al*., 2015). Chemical, biological, and physical approaches are used in decontamination strategies to reduce mycotoxins in food and feed commodities. Mycotoxins are converted via chemical reactions in chemical remediation strategies. While ammoniation, alkaline hydrolysis, peroxidation, ozonation, and the use of bisulphites are effective against one or more mycotoxins, a thorough understanding of the toxicity of eventual end products, as well as the impact on palatability and nutritional quality, is lacking (Vanhoutte *et al*., 2016)

Biological treatment methods include a variety of substances (algae, plant ingredients, etc.) that protect vital organs such as the liver and boost animal immune systems. Enzymatic or microbial detoxification also referred to as “biotransformation” or “biodetoxification” involves using microorganisms or their purified enzymes to catabolize the whole mycotoxin or to convert or cleave it into less or nontoxic compounds (Murugesan *et al*.,

2015). Some bacteria, such as *Rhodococcus erythropolis, Armillariella tabescens,* and *Myxococcus fulvus*, have been found to degrade AF in different ways. The ability to degrade ZEA was investigated in *Rhizopus oryzae, Bacillus licheniformis*, and *Pseudomonas sp.* (Alberts *et al*., 2006; Cao *et al*., 2013; Zhao *et al*., 2011; Varga *et al*., 2005; Yi *et al*., 2011). According to some reports, *B.subtilis* had protective effects against aflatoxicosis in layers and broilers fed naturally AF-contaminated diets and also healed ZEA toxicosis in pre-pubertal gilts when fed diets including ZEA. As a result, B. subtilis may have promising potential in feed industrial applications as a new feed additive for biodegradation of AF and ZEA (Jia *et al*., 2016).

Some physical processes aim to remove highly contaminated fractions from bulk material through sorting, milling, dehulling, cleaning, heating, irradiation or combinational approaches (Kaushik *et al*.,2015). Another physical removal strategy is the use of inorganic or organic mycotoxin binders (Kolosova *et al*., 2001). The widespread adoption of AF enterosorbents by the farm animal industry has led to the introduction of a variety of diverse materials and/or complex mixtures for AF binding, due to low feed inclusion requirements and easy management of these products. Mycotoxin enterosorbents, binders, sequestrants, interceptor molecules, trapping agents, adsorbents, toxin sorbents, and other words have been used to describe them. Smectite clays, zeolites, kaolinite, mica, silica, charcoal, sodium bentonite, and various biological constituents such as chlorophyllins, yeast products, lactic acid bacteria, plant extracts, and algae are reported to be present in these materials. Some contain natural or synthetic surfactants attached to smectite or zeolite minerals, resulting in hydrophobic organoclays or organozeolites (Eraslan *et al*., 2004; Ortatatli *et al*., 2001). Smectite clays appear to be the most powerful AF enterosorbents, according to data. While these adsorbing binders have others promising characteristics, some may have negative nutritional consequences due to vitamin and mineral binding or by decreasing antibiotic efficacy pharmacokinetics (Rosa *et al*., 2001). Furthermore, binding agents' adsorption efficacy is limited to a few mycotoxins, such as AF, ergot alkaloids, and a few other fungal toxins, although trichothecenes have been shown to be ineffective (Vekiru *et al*., 2007). As a result, alternative approaches to effective mycotoxin detoxification are needed.

Microorganisms and their particular products, such as enzymes, can be used to detoxify nonadsorbable mycotoxins as well as all other toxins for which respective microbes can be extracted from nature. Many microorganisms have been extracted from various environments, including animals' gastrointestinal tracts (GITs), soil, mycotoxin-contaminated materials (e.g., grains), and insects feeding on these materials. A recent analysis looked at the ability of various bacteria, yeast, fungi, and enzymes to detoxify mycotoxins through transformation, cleavage, and catabolization (Mc Cormick, 2013). These microorganisms or enzymes need to fulfill many different requirements before they can be used for gastrointestinal detoxification of mycotoxin in animals, such as:

- The microorganism and its reaction products need to be non-toxic and safe.
- High detoxification reactivity.
- Good technological properties (fermentation, downstream processing, stabilization).
- High stability in feed and during feed processing.
- No negative impact on feed (ingredients).
- Compatibility and stability in the GIT.
- Detoxification reaction in the GIT needs to be fast and as complete as possible.

Trichosporon mycotoxinivorans, a yeast strain capable of detoxifying OTA and ZEN, is one of the microorganisms that has been further evolved for functional use (Molnar *et al*., 2004). This yeast has been shown to detoxify OTA when used in poultry diets. An anaerobic rumen bacterium, BBSH 797 (Genus Novus of the family Coriobacteriacae, formerly Eubacterium), was isolated and grown as a trichothecene-detoxifying feed additive (Schatzmayr *et al*., 2006). Trichothecenes are detoxified by BBSH 797 by cleaving the 12, 13 epoxide ring, resulting in deepoxy trichothecenes.

One common approach to overcoming mycotoxicosis in poultry is to use herbal products, including essential oils, as plant-based fumigants in feed storage (Prakash *et al*., 2015). Essential oils are complex compounds with varying chemical compositions and concentrations of various compounds. Essential oils are divided into two classes, terpenes and phenylpropenes, based on the number of 5 carbon building blocks in each. For example, in commercial broilers, 500 ppm of ethanolic extract of Thymus vulgaris could partially reverse the negative effects of AFB1 (600 ppb). They proposed that this herb be used as a natural nonantibiotic feed additive to avoid aflatoxicosis in broilers. The levels of drug-metabolizing enzymes (phase I and phase II) are predicted to change as a result of a change in diet (nutrients, phytochemicals, pollution, xenobiotics), which will ultimately lead to a change in AFB1 adducts. Because phenolic phytochemicals have varying degrees of antioxidant activity due to their chemical structures, they are thought to play a protective role in cellular components against free radical—induced damage caused by aflatoxicosis (Abdel-Wahhab *et al*., 2010). A herbal mycotoxin binder composed of minerals (extra purified clay containing diatomaceous earth minerals), antioxidants (curcuminoids extracted from turmeric), and enzymes in proportions of 15, 10, and 75%, respectively, partially restored feed consumption and egg production, alleviating some side effects of AFB1 (500 ppb in feed) in broiler breeders (Manafi *et al*., 2013).

4.2 DIAGNOSIS AND TREATMENT

4.2.1 Diagnosis

- Mycotoxicosis can be suspected when the history, signs, and lesions are suggestive of feed intoxication and when moldy ingredients or feed are evident**.**

Toxin exposure associated with the consumption of a new batch of feed may result in subclinical or transient disease. Chronic or intermittent exposure can occur in regions where grain and feed ingredients are of poor quality and when feed storage is substandard or prolonged. Impaired production efficiency can be a clue to a mycotoxin problem, as can improvement due to correction of feed management deficiencies. Oral ulcers and crusts occurring on the palate or tip of the tongue occur with exposure to mycotoxins, including aflatoxin and mycotoxins produced by *Fusarium* (Federic *et al*., 2019).

- Definitive diagnosis of mycotoxicosis involves detection and quantitation of the specific toxin(s).

This can be difficult because of the rapid and high-volume use of feed and ingredients in commercial flocks. Diagnostic laboratories differ in their respective capability to test for mycotoxins and should be contacted before sending samples. Poultry that are sick or recently dead should be submitted for testing with a representative feed sample. A necropsy and related diagnostic tests should accompany feed analysis if mycotoxicosis is suspected. Concurrent infectious or parasitic disease may occur. Sometimes, a mycotoxicosis is suspected but not confirmed by feed analysis. In these situations, a complete laboratory evaluation can exclude

other significant diseases (Federic *et al.*, 2019).

- Feed and ingredient samples should be properly collected and promptly submitted for analysis**.**

Mycotoxin hotspots may occur in a batch of toxic feed or grain. Multiple samples taken from different sites increase the likelihood of confirming mycotoxin presence.

Samples should be collected at sites of ingredient storage, feed manufacture and transport, and feed bins and feeders. Fungal activity increases as feed moves from the feed mill to the feeder pans. Test samples of 500 g (1 lb) should be transported in clean paper bags that are properly labeled. Sealed plastic or glass containers should only be used for short-term storage and transport, because feed and grain rapidly deteriorate in airtight containers (federic *et al.*, 2019).

Table 4: showing treatment of mycotoxin infection

NAME	SUMMARY	SOURCE
Supportive care	Isolate the bird from the flock and place in a safe, comfortable, warm location (your own chicken "intensive care unit") with easy access to water and food. Limit stress. Call your veterinarian	
Probiotics	Have showed benefit at reducing the harmful effects of mycotoxins	Ferrer *et al.*, 2015
Sea buckthorn *(Hippophae rhamnoides)*	Berries, leaves, juice and oil have shown to be of benefit in reducing the harmful effects of mycotoxins in the diet	Ramasamy *et al.*, 2010
Vitamins E and C	Oral supplementation of additional vitamins might partially counteract the toxicity of infection with multiple mycotoxins	Ahmadi *et al.*, 2015; Salimian *et al.*, 2014; Weber *et al.*, 2007; Rizzo *et al.*, 1994
Banana peel	Dried banana peel added to feed	Shar et al., 2016
Turmeric extract (Curcuma longa)	5 mg/kg in feed has shown to provide protection against the toxic effects of aflatoxins on the chicken's liver and kidney	Gholami-Ahangaran et al., 2015; Rangsaz et al., 2011

Bacillus subtilis	1000g/t added to diet helps offset the negative effects of mycotoxins	Jia et al., 2016; Fan et al., 2013 See more at: http://www.poultrydvm.com/condition/mycotoxicosis
Black cumin (Nigella sativa)	2-5% added to feed	Khan et al., 2013; Aydin et al., 2008
Yeast extract (Saccharomyces cerevisiae)	1 g/kg added to diet	Matur et al., 2011; Matur et al., 2010
Neutral electrolyzed oxidizing water (NEW)	Soaking contaminated foods in 60mg/L available chlorine, pH 7.01) for 15 minutes at room temperature	Jardon-Xicotencatl et al., 2015
Mycofix Select	Provides some protective effects against the toxins	Lee et al., 2012
Beer fermentation residue (BFR)	1% of feed, reduced severity of the effects of aflatoxins	Bovo et al., 2015
Selenite	Adding sodium (0.6 mg/kg)	Chen et al., 2014
Rosemary (Rosmarinus officinalis)	500 ppm extract	Manafi et al., 2014

Sources: http://www.poultrydvm.com/condition/mycotoxicosis

5.0 CONCLUSION AND RECOMMENDATION

It's become important to consider the frequency and incidence of mycotoxins, as well as their individual and combined harmful effects on poultry performances. In the field, new insights on actual microbial detoxification routes are required, which could be based on the biodegradation metabolisms of non-mycotoxins found in diverse microbial communities. The use of cutting-edge analytical techniques such as liquid chromatography tandem mass spectrometry would improve the precision of determining multiple mycotoxins present in agricultural commodities at the same time. The latest enzymatic deactivation technologies aid in the removal of mycotoxins that are resistant to binding with binder materials. To have general guidelines for reducing these adverse contaminants and avoiding re-contamination, research on the stability of toxins in the entire "farm to fork" chain is required. The additives' effectiveness against various mycotoxins and livestock must be demonstrated, for example, by peer-reviewed studies. Overall, mycotoxins continue to pose a major threat to the poultry industry, and researchers around the world are still searching for new ways to avoid them.

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