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Effects of Mycotoxins in Animal Nutrition: A Review

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ABSTRACT

Mycotoxins are low molecular weight secondary metabolites produced by certain strains of filamentous fungi such as *Aspergillus*, *Penicillium* and *Fusarium*, which invade crops in the field and may grow on foods during storage under favourable conditions of temperature and humidity. They are regularly implicated in toxic syndromes in animals and humans. No region of the world escapes the problem of mycotoxins and its estimated that there are about 300 harmful mycotoxins. Food and Agricultural Organisation (FAO) estimates that about 25% of the world crops contain mycotoxins. Mycotoxins have been detected in various food commodities from many parts of the world and are presently considered as one of the most contaminants of food and feed. Mycotoxins causes mycotoxicoses and their toxicity depends on the amounts ingested, time-span of exposure, type of animal, their breed, age, sex, health status, but also other parameters such as density of animals, diseases and temperature. The mycotoxins of most concern due to their toxicity and occurrence are aflatoxin, vomitoxin, ochratoxin, zearaleone, fumonisin and T-2 toxins. They cause significant economic losses in animals due to reduced productivity, increased disease incidence, chronic damage of vital organs and decreased reproductive performance. Also, the productivity and nutritive value of infected grains and cereals drops after contamination by mould. Animals may have varying susceptibilities to mycotoxins depending on physiological, genetic and environmental factors. Preventing mould growth and subsequent mycotoxin production is essential to the feed manufacturer, livestock producer and for maximum animal performance.

Key words: Mycotoxins, animal feed, moulds, animal nutrition

INTRODUCTION

Mycotoxins are low molecular weight secondary metabolites produced by certain strains of filamentous fungi such as *Aspergillus*, *Penicillium* and *Fusarium*, which invade crops in the field and may grow on foods during storage under favourable conditions of temperature and humidity. They are regularly implicated in toxic syndromes in animals and humans (Smith *et al*., 1995; Berry, 1998; Charoenpornsook and Kavisarasai, 2006). Due to the diversity of their toxic effects and their synergetic properties, mycotoxins are considered as risky to the consumers of contaminated foods and feeds (Yiannikouris and Jonany, 2002; Omede, 2008).

Mycotoxins have been detected in various food commodities from many parts of the world and are presently considered as one of the most dangerous contaminants of food and animal feed (CAST, 1989; Okoli, 2005; Okoli *et al*., 2006a, b, 2007a, b). No region of the world escapes the

problem of mycotoxins and according to Lawlor and Lynch (2005) and Okoli *et al.* (2006b), mycotoxins are estimated to affect as much as 25% of the world's crops each year. Mycotoxins are produced only under aerobic condition (Ratcliff, 2002). Adverse effects on animal health and production have been recognized in intensively farmed animals such as poultry, swine and cattle as a consequence of the consumption of high levels of cereals and oilseeds in the diet (Smith and Anderson, 1991; Smith *et al.*, 1994; Charoenpornsook and Kavisarasai, 2006). Animals may have varying susceptibilities to mycotoxins depending on physiological, genetic and environmental factors. Most mycotoxins such as aflatoxin B_1, T-2 toxin and ochratoxin A inhibit protein synthesis (Charoenpornsook and Kavisarasai, 2006). This inhibition may not be the primary mechanism involved in their immunotoxic effects. They may have selective effects on various target organs, affect membranes or interfere with macromolecular synthesis and function. They can directly or indirectly influence immunological functions. Some of the mycotoxins are neurotoxic or cause other organ pathology and these compounds may activate endocrine mechanisms (e.g., stress-induced release of corticosteroids inhibits immune function (Sharma, 1993)).

Mycotoxins occur sporadically both seasonally and geographically. The formation of mycotoxins in nature is considered a global problem, however, in certain geographical areas of the world, some mycotoxins are produced more readily than others (Devegowda *et al.*, 1998; Ratcliff, 2002; Lawlor and Lynch, 2005). Table 1 shows the mycotoxin that may be found in feeds that come from different global locations. They occur naturally in a wide variety of feedstuffs used in animal feeds. In most European countries aflatoxins are not considered to be a major problem. In contrast, vomitoxin, ochratoxin, zearalenone are found more frequently. Aflatoxins are common in humid climatic conditions like those existing in Asian and African countries and certain parts of Australia (Cortyl, 2008). The problem of mycotoxins does not just end in animal feed or reduce animal performance; many become concentrated in meat, egg and milk of animal and can pose a threat to human health (Akande *et al.*, 2006). Some examples of foods, of animal origin which may be naturally contaminated with mycotoxins are shown in Table 2.

Effects of major mycotoxins in poultry and swine

Aflatoxins: Aflatoxins are fluorescent compound, they are chemically classified as difurocoumarolactones and their biosynthesis by the producing fungi is via polyketide pathway (Smith and Moss, 1985; Akande *et al.*, 2006). Aflatoxins are the most well known mycotoxins and extensive research has been done about these mycotoxins. There are four major aflatoxins produced in feedstuffs: Aflatoxin B_1, Aflatoxin B_2, Aflatoxin G_1 and Aflatoxin G_2. Today, it is agreed that

Table 1: Geographic occurrence of mycotoxins

Locations	Mycotoxins
Western Europe	Ochratoxin, vomitoxin, zearalenone
Eastern Europe	Zearalenone, vomitoxin
North America	Ochratoxin, vomitoxin, zearalenone, aflatoxins
South America	Aflatoxins, fumonisins, ochratoxin, vomitoxin, T-2 toxin
Africa	Aflatoxins, fumonisins, zearalenone.
Asia	Aflatoxins
Australia	Aflatoxins, fumonisins

Source: Devegowda *et al.* (1998)

Table 2: Some food of animal origin which may be naturally contaminated with mycotoxins

Mycotoxins	Potential effects on humans	Occurrence	Maximum level reported (ppb)
Aflatoxin B_1	Hepatic cancer	Eggs	0.4
		Pig liver	0.5
		Pig muscle	1.04
		Pig kidney	1.02
Aflatoxin M_1	Carcinogenic	Cow milk	0.33
Ochratoxin A	Renal damage	Pig liver	98
		Kidney	89
		Sausages	3.4
Zearaelenone	Oestrogenic	Pig liver	10
		Pig muscle	10

Source: FAO (1998)

only four species of fungi produce aflatoxins. They are namely, *Aspergillus flavus*, *Aspergillus parasiticus*, *Aspergillus nomius* and *Aspergillus pseudotamarii* (Kurtzman *et al*., 1987; Payne, 1998; Ito *et al*., 2001; Cortyl, 2008). However, only *A. flavus* and *A. parasiticus* are economically important.

Aflatoxins are produced when adequate substrate and favourable environmental conditions are present (tropical and subtropical climates, humid storage conditions). While young animals are most susceptible to the effects of aflatoxin, all ages are affected. Aflatoxin causes a variety of symptoms depending on the animal, dose, length of exposure, species, breed and diet or nutritional status. However, in all animals, aflatoxin can cause liver damage, gastrointestinal dysfunction, reduced productivity, decreased feed utilization and efficiency, decreased reproductive performance, reduced milk or egg production, embryonic death, teratogenicity (birth defects), tumours and suppressed immune system function, even when low levels are consumed (Jones *et al*., 1994; Cortyl, 2008). According to Devegowda *et al*. (1998), aflatoxins are immune-suppressors and have different effects on pigs, varying from poor growth rates in weaners and finishers to abortion and agalactia in sows. Reports have that the first sign of an aflatoxin problem is decreased feed intake and depending on the levels present, losses can result from deaths, reduced growth rates, poor feed conversion efficiency and carcass condemnations. Levels in excess of 0.5ppm in the diet of lactating sows will reduce piglet growth rates due to aflatoxins in milk. For grower/finisher pigs reduced growth rates can be expected at concentrations in excess of 0.2 ppm (Devegowda *et al*., 1998).

In poultry, ducks are the most sensitive to aflatoxins, followed by turkey, broiler and layers. Duration of exposure, as well as age, is as important as the level of aflatoxins in feed. The following symptoms have been observed following contamination with aflatoxins in poultry: fatty liver, kidney disorders, leg and bone problems, pigmentation problems (carcasses, egg yolk), reduced hatchability, smaller eggs and reduced eggshell quality, coccidiosis, vaccine failure, reduced immunity, lower resistance to diseases, bacteria, viruses and of course reduced performance (Cortyl, 2008).

Dersjant-Li *et al*. (2003) studied the impact of low concentrations of aflatoxin, deoxynivalenol or fumonisins in diets on growing pigs and poultry. In this study, they used simple linear regression to summarize different trials from the literature and estimated the relationship between mycotoxin level and for example, growth rate. The researchers estimated that for each additional part per million (ppm) of aflatoxin in the feed, the growth rate of pigs is depressed by 16%. For instance, a level of 0.3 ppm aflatoxin in feed would result in a 5% reduction in daily weight gain when

compared to a non contaminated feed. For deoxynivalenol, the reduction in daily weight gain was estimated at about 8% for each additional ppm. Similarly, it was calculated that growth performance of pigs is reduced by 0.4% for each additional ppm of fumonisins in the diet.

Ochratoxins: They are metabolites produced by certain species of the genera *Aspergillus* and *Penecillium* (Wood, 1992). Ochratoxin A (OTA or OA) is the major metabolite of toxicological significance and it is mainly a contaminant of cereal grains. There are other compounds in this group, but they are less toxic. *Aspergillus ochraceus* produces OTA in hot climates, while *Penicillium verrucosum* produces it in temperate countries.

Ochratoxin A is teratogenic in rat, hamster and chick embryo and is an inhibitor of hepatic mitochondrial transport systems (Akande *et al*., 2006). Ochratoxin A is a nephrotoxin and has also been reported to cause damage to the liver, gut, lymphoid tissue and renal tubular damage particularly at higher doses (Harwig *et al*., 1974). In poultry, OTA is often reported to have damaging effects and symptoms are increased mortality, reduced growth and decreased feed conversion ratio and feed refusal. At higher doses, one can observe diarrhoea, tremors and other neural malfunctions (Cortyl, 2008). In laying birds, OTA also reduces egg production and quality (Cortyl, 2008).

Gentles *et al*. (1999) have demonstrated the negative effect of 2.5 ppm of OTA in feed of young broiler chickens. After 3 weeks, their body weights were reduced by 23% when compared to controls, while feed conversion ratio was comparable. Stoev *et al*. (2002) observed a dramatic effect of 5 ppm on bodyweight of chicks (-61% after 42 days) while a level of 1 ppm resulted in a loss of 18%.

In pigs, OTA causes a typical disease called porcine nephropathy (kidney damage). This can result in rejection of carcasses at the slaughter house. Indeed, OTA has an affinity with serum proteins (it is bound to them), which makes it quite stable. It can be found in pig meat and meat products. OTA also affects fertility of boars. It crosses the placental barrier and can affect the development of foetuses. Tail necrosis sometimes observed in newborn piglets is often associated with OTA (Cortyl, 2008).

Zearalenone: Also called ZON, Zea, or ZEN. It is a non-steroidal estrogenic mycotoxin produced by Fusarium fungi, mainly *Fusarium graminearum* (*Gibberella zeae* and *Fusarium culmorum*) (Marasas *et al*., 1984). It mimics the effects of the female hormone, oestrogen (Okoli *et al*., 2008). At high concentrations (1-30 ppm), it can interfere with ovulation, conception, implantation and foetal development. In pregnant sows it can increase the incidence of abortions and still births, reduce litter size and piglet viability. It may increase the weaning to service interval (Jones *et al*., 1994). Young gilts are most sensitive, with concentrations as low as 0.5 to 1 ppm causing pseudo-oestrus and vaginal or rectal prolapse. The most striking clinical feature is the swollen red vulva of immature gilts. Young boars may have reduced libido and decreased testicular size but mature boars are rarely affected (Jones *et al*., 1994).

In poultry, Cortyl (2008) reported that Zearalenone appears to be well tolerated by poultry. Chi *et al*. (1980) observed that a single oral ingestion of 15 g kg^{-1} bodyweight was not toxic. Allen *et al*. (1981) reported that up to 800 ppm of ZON in feed from 6-9 weeks of age does not affect performance of broilers. Allen *et al*. (1983) reported the opposite for turkey. He observed reduced egg production (-20%) with 100 ppm for 56 days.

Tricothecenes: This is a group of toxic fungal metabolites based on the structure (6) and which are produced by a number of species of the genus *Fusarium*. Trichothecenes are divided in 2 groups. Group A trichothecenes include T-2 toxin, HT-2 toxin and diacetoxyscirpenol (DAS). Common group B trichothecenes are deoxynivalenol (DON or vomitoxin), nivalenol (NIV) and Fusarenon X. T-2 toxin has been the most extensively studied tricothecene in poultry and it has been found that the primary effect of T-2 toxicosis in young broiler chicks is oral necrosis (Jewers, 1990). The ability of the three tricothecenes, diacetoxyscirpenol, croticin and T-2 toxin, to cause oral necrosis and to affect bodyweight gain has been studied in growing chicks. Jewers (1990) reported that at a dietary inclusion rate of 5 ug g^{-1} of diacetoxyscirpenol, a bodyweight reduction of 24% resulted, whereas T-2 toxin produced an 11% reduction at the same incorporation rate. A more severe oral response was observed with diacetoxyscirpenol. No effect on bodyweight gain or oral inflammation or necrosis was observed with croticin fed at10 ug g^{-1}. It is generally regarded that the presence of oral lesions in poultry is the primary means of diagnosing tricothecene toxicoses in the field.

Dietary T-2 toxin has also been found to affect the nervous system by producing an abnormal positioning of the wings, hysteroid seizures, or an impaired righting reflex. In addition, it can induce abnormal feathering, drastically decrease feed intake without impairing feed efficiency, decrease egg production and cause thinning of egg shells and destruction of the haemotopoietic system (Wyatt, 1979). Jones *et al.* (1994) reported that T-2 toxin has been implicated to cause mouth and intestinal lesion as well as impair the bird=s immune response, causing egg production declines, decreased feed consumption, weight loss and altered feather patterns. Turkeys are also very sensitive to T-2 toxin (reduced growth, beak lesions, reduced immunity). Kubena *et al.* (1987) reported that DON at 18 ppm in feed of Leghorn chickens did not affect their weight gain. However, nivalenol was reported to have negative effects in poultry. Hedmand *et al.* (1995) studied the effect of different doses of NIV in feed of 7 day old male broiler chickens. Bodyweight gain was reduced by 11% for levels of 6 and 12 ppm, while at lower doses no effect was observed. Feed intake and feed conversion ratio were also affected. Gizzard erosions were found in one third of the birds given a feed containing 12 ppm NIV and in 8% of those fed 3 or 6 mg kg^{-1}. Such damages were not observed in the control group. Also, absolute and relative liver weights were reduced with levels of 6 and 12 ppm. Garaleviciene *et al.* (2002) studied the effects of NIV in laying hens. For 7 weeks, White Leghorn hens (55 weeks old) were given access to diets containing 0, 1, 3 or 5 ppm NIV. Feed intake was reduced by NIV, but there were no apparent effects on bodyweight, egg production and egg quality. However, pathological examination of the birds at the end of the trial revealed that 40 to 75% of hens fed a diet containing NIV (3 and 5 ppm) had gizzard lesions, haemorrhages in the duodenum and swollen cloaca and oviducts with immature eggs. Some of the birds in the 1 ppm NIV group had light and fragile livers.

Deoxynivalenol and T-2 toxin appear as the most harmful trichothecenes in pigs. T-2 toxin and other type A Trichothecenes causes reduced productivity at feed concentrations of 200 ppb or less. In sows, infertility with some lesions in the uteri and ovaries can be observed after a feed contaminated with 1 to 2 ppm of T-2 toxin has been consumed. DON causes a disease called moldy corn toxicosis of swine. The grain is unpalatable to pigs; feed intake is reduced and results in poor weight gain or even weight loss, increased incidence of infectious diseases and digestive disorders (Cortyl, 2008). In the farrowing house, DON causes failure of mature sows to return to oestrus, reduced efficiency, but also intestinal tract inflammation and acute diarrhoea of suckling piglets, resulting in high mortality (Cortyl, 2008). Etienne *et al.* (2006) also observed the negative effect

of DON in sow feed during lactation. When comparing a control group to a group of sows fed with a diet containing 2 ppm of DON, they observed that the feed intake was depressed by 21% on the whole lactation period. As a result, daily weight gain of the piglets was less in the contaminated group (237 vs. 274 g day^{-1}) even if the difference was not significant due to high variability. The sows eating the feed containing the mycotoxin lost more body weight (25.8 kg vs. 17.5 kg) during lactation than their counterparts. This is of course primarily due to their lower feed intake.

Fumonisins: The fumonisins are a group of compounds originally isolated from *Fusarium moniliforme* (Gelderblom *et al*., 1988). Six different fumonisins (FA_1, FA_2, FB_1, FB_2, FB_3 and FB) have been reported, the A series are amides and the B series have a free amine (Gelderblom *et al*., 1992). In most animals fumonisin impairs immune function, causes liver and kidney damage, decreases weight gains and increases mortality rates. It also causes respiratory difficulties in swine (Jones *et al*., 1994). The fumonosins (FB_1 and FB_2) have been isolated from *Fusarium moniliforme* cultures and found to promote cancer in rats (Gelderblom *et al*., 1988). These toxins occur naturally in corn and have been associated with equine leukoencephalomalacia (Ross *et al*., 1990). They often happen jointly with other mycotoxins (aflatoxins, DON and ZON).

In poultry, relatively high levels are required to observe negative effects of fumonisins (Cortyl, 2008). Broomhead *et al*. (2002) report that feed intake, body weight gain and feed conversion of chicks were not affected by fumonisin B_1, despite levels of 25 or 50 ppm was used. Ledoux *et al*. (1992) observed that levels of 100 to 400 ppm were detrimental to the performances in the case of day-old chicks. Kubena *et al*. (1987) studied the effects of fumonisin B_1, combined or not with Diacetoxyscirpenol and OTA in Turkey. Reduced weight gain was observed with 300 ppm of fumonisin B_1. The reduction was 30% after 3 weeks when compared to control. The feed conversion ratio was also affected. Since the toxicity of fumonisins and DAS (or fumonisins and OTA) appeared to be additive, the authors stated that even if a level of 300 ppm is very unlikely under practical conditions, combinations of different mycotoxins at lower levels might put poultry at risk.

In pigs, the main symptom of fumonisin B_1 exposure is called PPE (porcine pulmonary oedema) which affects lungs and heart. At lower levels, liver and pancreas damage can be observed, as well as immunosuppression. Production parameters can also be affected: reduced weight gain (above 2 ppm), increased FCR and reduced performances (Cortyl, 2008).

Effects of mycotoxins on ruminants: Ruminants such as cattle, sheep, goats and deer are less known for their sensitivity to the negative effects of mycotoxins than are non-ruminants. However, production (milk, beef, or wool), reproduction and growth can be altered when ruminants consume mycotoxin-contaminated feed for extended periods of time (Hussein and Brasel, 2001). Beef and dairy cattle, sheep, goats and deer are among ruminants that have been investigated. Acute aflatoxicosis in cattle has been thoroughly described. Clinical signs consist of reduced feed consumption, dramatic drops in milk production, weight loss, liver damage and reduced immune system function and rumen metabolism in cattle (Bodine and Mertens, 1983, Lawloy and Lynch, 2001). Increasing AF in cattle feed to levels such as 10, 26, 56.4, 81.1 and 108.5 μg kg^{-1} has been shown to significantly reduce feed intake at each level in a dose-dependent manner (Choudhary *et al*., 1998). In a 155 day feeding trial, AFB_1 (600 μg kg^{-1}) was shown to depress feed efficiency and rate of gain in steers (Helferich *et al*., 1986). Decreased feed efficiency in cattle has been attributed to compromised ruminal function by reducing cellulose digestion, volatile fatty acid production and rumen motility (Cook *et al*., 1986; Helferich *et al*., 1986; Diekrman and Green,

1992). Several mechanisms of bovine immunosuppression by AFB_1 have been illustrated *in vitro*. Paul *et al.* (1977) demonstrated that AFB_1 suppressed mitogen-induced stimulation of peripheral lymphocytes. In another study of Bodine *et al.* (1984), AFB_1 was shown to inhibit bovine lymphocyte blastogenesis. In a study by Cook *et al.* (1986), radio telemetry was used to measure rumen motility in cattle and the results showed that AF administration (200-800 μg kg^{-1}) slowed rumen motility in a dose-dependent manner. Ochratoxins, on the other hand, do not cause significant toxicity to cattle when fed alone in naturally occurring doses. Barley naturally-contaminated with OTA (390-540 μg kg^{-1}) and low levels of AFB_1 (12-13 μg kg^{-1}) did not induce any significant clinical symptoms in 12 week-old calves. The absence of a toxic effect may have been due to the ruminal microbial degradation and detoxification (Patterson *et al.*, 1981). Chronic exposure of a dairy herd to aflatoxin contaminated corn (120 ppb) resulted in severe herd health problems, including the birth of small, unhealthy calves, diarrhoea, acute mastitis, respiratory disorders, prolapsed rectum, hair loss and reduced feed consumption (Charoenpornsook and Kavisarasai, 2006). Aflatoxins also affect the quality of milk produced by dairy cows and result in carry-over of AFM_1 from AF-contaminated feed (Applebaum *et al.*, 1982). In the study by Applebaum *et al.* (1982), 10 ruminally-canulated lactating Holstein cows were given AFB_1 (13 mg per cow daily) via the rumen orifice for 7 days. Levels of AFM_1 in the milk of the treated cows ranged from 1.05 to 10.58 ng L^{-1}. The AFB_1-treated cows also had a significant reduction in milk yield. In another study of Veldman *et al.* (1992), the carry-over rate was shown to be higher (6.2 vs. 1.8) in early lactation (2-4 week) when compared with late lactation (34-36 week).

The T-2 toxin is also believed to induce immunosuppression in cattle (Black *et al.*, 1992) by decreasing serum concentrations of IgM, IgG and IgA (Mann *et al.*, 1983), neutrophil functions and lymphocyte blastogenensis (Mann *et al.*, 1984) and the response of lymphocytes to phytohemagglutinin (Mann *et al.*, 1984). This toxin was also shown to induce necrosis of lymphoid tissues (Buening *et al.*, 1982). Bovine infertility and abortion in the final trimester of gestation also have resulted from consumption of feed contaminated with T-2 toxin (Placinta *et al.*, 1999). Calves consuming T-2 toxin at 10-50 mg kg^{-1} of feed have demonstrated ulcers in the abomasums and sloughing of the papilla in the rumen (Cheeke, 1998a). A case investigation of dairy cattle fed moldy corn containing 1 mg kg^{-1} T-2 toxin resulted in hemorrhagic syndrome (Hsu *et al.*, 1972). With the exception of T-2 toxin, cattle have not been adversely affected by tricothecenes (Helferich *et al.*, 1986). Neither DON nor DAS are known to affect cattle health or performance in the feedlot (Dicostanzo *et al.*, 1996). Charmley *et al.* (1993) has shown that DON at levels as high as 6 mg kg^{-1} of feed had no adverse effects on milk yield and did not show evidence of carry-over into milk. Zearelenone has been suggested as a causative agent of infertility, reduced milk production and hyperestrogenism in cattle (D'Mello and MacDonald, 1997). Fescue foot, hyperthermia and fat necrosis in cattle have been linked to consumption of tall fescue parasitized with *Acremonium coenophialum* (Cheeke, 1998b). Cattle consuming tall fescue contaminated with endophytic fungi such as *A. lolii* also have shown symptoms of staggers, excitability, increased rectal temperature, increased respiration rate and loss of body weight (Ross *et al.*, 1989).

Early studies suggested sheep as the most resistant species to mycotoxicosis (Hussein and Brasel, 2001). Wogan, (1966) illustrated a high LD_{50} (500 mg kg^{-1}) in ovine's fed AF. However, lower LD_{50} of AF (e.g., 2 mg kg^{-1}) have been established (Miller and Wilson, 1994) by injection of AF in sheep. As reviewed by Hussein and Brasel, (2001), several studies, however, have shown notable effects of AF on sheep. Harvey *et al.* (1995) showed that feeding diets contaminated with AF (79% AFB_1, 16% AFG_1, 4%% AFB_2 and 1% AFG_2) to ewe lambs (2.5 or 5.0 mg kg^{-1} of feed for

35 days) resulted in hepatotoxicity. In another study (Fernandez *et al*., 1997), lambs fed AF at 2.5 mg kg^{-1} of feed daily for 21 days showed symptoms of clinical aflatoxicosis including hepatic and nephritic lesions, altered mineral metabolism and increased size and weight of the liver and kidney. Another study of Ramos *et al*. (1996) with the same daily dose of AF (2.5 mg kg^{-1} of feed) examined the plasma mineral concentrations on day 1, 2, 4 and 8 of the initial dose. On day 4 of intoxication, significant reductions in plasma mineral concentrations were detected for Ca (2.39 vs. 2.06 mM), P (2.95 vs. 2.50 mM), Mg (0.88 vs. 0.77 mM), K (4.40 vs. 3.81 mM) and Zn (13.2 vs. 11.6 μM). The resulting mineral deficiencies due to aflatoxicosis were attributed to lower feed intake and to the liver and kidney malfunctions as a result of AF intoxication. Exposure of lambs to AF (2.5 mg kg^{-1} of feed for 3 week) revealed changes in extrinsic coagulation factors as determined by increased fibrinogen concentration (Fernandez *et al*., 1995). In a study by Fernandez *et al*. (2000), 5 month old lambs were given feed contaminated with AF (2 mg kg^{-1} of feed) for 37 days. Average daily gain on day 35 of feeding AF was significantly reduced from 125 to 79 g and the exposed lambs showed decreased cellular immunity. After allowing for a clearance period of 30 days, the AF-exposed lambs had average daily gain and cellular immunity similar to those for the controls. Mechanisms for cellular immune response to AF in sheep have not been elucidated. Contrary to *in vitro* findings indicating inhibition of bovine lymphocyte blastogenesis by AF (Bodine *et al*., 1984). Edrington *et al*. (1994) could not prove that ovine mitogen-induced lymphocyte blastogenesis occurs *in vivo*. *Fusaria* mycotoxins at high doses also appear to have some negative effects on sheep. Exposing sheep to DON (15.6 mg kg^{-1} of feed) for 28 days had no effects on average daily gain, hemacytology parameters, or liver function (Harvey *et al*., 1986). However, weight loss (-0.6 vs. 2.4 kg day^{-1}) was reported after 34 days of feeding DAS (5 mg kg^{-1} of feed) to lambs. Further weight loss (-2.7 vs. 24 kg day^{-1}) also was reported at 34 days of feeding lambs same level of DAS in combination with AF (2.5 mg kg^{-1} of feed) suggesting a synergistic effect (Harvey *et al*., 1995). It has been suggested that high dietary levels (12 mg kg^{-1} of feed) of ZEN for extended periods of time (10 days) may affect reproductive performance of sheep negatively by reducing fertility and ovulation rates (Dicostanzo *et al*., 1996). Fumonisins at high doses (11.1-45.5 mg kg^{-1} of body weight) have been demonstrated as acutely and fatally nephrotoxic and hepatotoxic in lambs (Edrington *et al*., 1995). Perennial rye grass staggers have been observed in sheep consuming rye grass contaminated with *A. lollii*. Symptoms have included shaking with loss of coordination and inability to walk (Cheeke, 1998b). Staggers have been demonstrated when *A. lolii*-contaminated rye grass had lolitrem B toxin at levels of 2.0-2.5 mg kg^{-1} (DiMenna *et al*., 1992).

Ruminants other than cattle and sheep have shown variable resistance to mycotoxins (Hussein and Brasel, 2001). Levels of AF at 95 mg kg^{-1} of feed offered to weanling goats had no effects on bodyweight gain and did not show any noticeable signs of toxic effects (Gurung *et al*., 1998). Signs of toxic effects were only detected through serum profile and sphingolipid analysis. In a study with white-tailed deer fawn fed 800 mg kg^{-1} AF over an 8 week-period (Quist *et al*., 1997), acute injuries in the liver were indicated by increased serum bile acid concentrations and hepatic lesions.

Economic impact of mycotoxins: Mycotoxins have significant economic and commercial impact, in that both the productivity and nutritive value of the infected cereal and forage is affected (Ratcliff, 2002). Also, its significant economic losses are associated with their impact on human health, animal productivity and both domestic and international trade. It is estimated that 25% of the world's food crops, including many basic foods, are affected by mycotoxin producing fungi.

According to FAO estimates global losses of foodstuffs due to mycotoxins are in the range of 1000 million tonnes per year.

The nutritive value of grains and cereals drops after contamination by mould. Contamination by moulds affects both the alimentary value and organoleptic characteristic of feed and entails a risk of toxicosis. The biological effects of mycotoxins depend on the ingested amounts, number of occurring toxins, duration of exposure to mycotoxins and animal sensitivity (Akande *et al*., 2006). Also mycotoxins can induce health problems that are specific to each toxin or affect the immune status of animals, favouring infections. This is the major reason for the difficulty of diagnosing mycotoxicoses (Yiannikouris and Jonany, 2002). Mycotoxins produce a wide range of harmful effects in animals. The economic impact of reduced animal productivity, increased incidence of disease due to immunosuppression, damage to vital organs and interference with reproductive capacity is many times greater than the impact caused by death due to mycotoxin poisoning (Akande *et al*., 2006). Mycotoxins in combination appear to exert greater negative impact on the health and productivity of livestock in comparison to their individual effects (Smith and Seddon, 1998).

There are multiple criteria for assessing the economic impact of mycotoxins on humans and on animal agriculture. Considerations include loss of human and animal life, health care and veterinary care costs, loss of livestock production, loss of forage crops and feeds, regulatory costs and research cost focusing on relieving the impact and severity of the mycotoxin problem (Hussein and Brasel, 2001). Formulas for worldwide economic impact have been difficult to develop and therefore, most reports on economic impact are on a single aspect of mycotoxin exposure or contamination (Hussein and Brasel, 2001).

Studies have shown extensive mycotoxin contamination in both developing and developed countries. Surveillance studies (Placinta *et al*., 1999) showed that worldwide contamination of cereal grains and other feeds with *Fusarium* mycotoxins is a global concern. In Yugoslavia, studies on mycotoxigenic fungi in raw milk have indicated that 91% of the samples tested were contaminated (Skrinjar *et al*., 1995). In the US, a study was conducted in seven Midwestern states in 1988-1989 and found mycotoxins in 19.5% of corn samples assayed prior to any induced environmental stress and 24.7% of the samples following stress induction (Russel *et al*., 1991). Shane (1994) estimated the 1980 losses due to AF in corn of eight South-Eastern states at 97 million dollars with additional 100 million dollars in production losses at hog farms feeding the contaminated corn.

In India, a study in the Bihar region from 1985 to 1987 (Ranjan and Sinha, 1991), nearly 51% of the 387 samples tested were contaminated with molds. Of the 139 samples containing AF, 133 had levels above 20 μg kg^{-1}. In another study (Phillips *et al*., 1996), levels as high as 3700 μg kg^{-1} of AF was reported in groundnut meal used for dairy cattle. Researchers also found 21 of 28 dairy feed samples from farms in and around Ludhiana and Punjab to be contaminated with AFB_1 at levels ranging from 50 to 400 μg kg^{-1} (Dhand *et al*., 1998). It was estimated that 10 million dollars were lost in India's export within a decade due to groundnut contamination with mycotoxins (Vasanthi and Bhat, 1998).

In Thailand, determination of mycotoxins showed that aflatoxin B1 was detected in 23/25 samples (92%) and the average was 7.56 ppb. Ochratoxin A was detected in 3/10 samples (30%) in levels of 10.48, 11.14 and 12.35 ppb. Deoxynivalenol was detected in 13/15 samples (86%) and the average was 33.77 ppb. T-2 toxin was detected in all samples (10 samples) and the average was 6.91 ppb. Extent of mycotoxins contamination was determined from 10 samples. The results

revealed that 3 out of 10 samples were contaminated with 4 mycotoxins (aflatoxin B_1, ochratoxin A, deoxynivalenol and T-2 toxin) and 7 out of 10 samples were contaminated with 3 mycotoxins (aflatoxin B_1, deoxynivalenol and T-2 toxin) (Charoenpornsook and Kavisarasai, 2006).

These results suggest a high risk for human health because of the possibility of indirect exposure through meat and other products from animals consuming contaminated feedstuffs.

CONCLUSION

It is clear that mycotoxins will be of increasing importance for all those involved in feed manufacturing, farming and food production. Mycotoxins are harmful to animals and can greatly affect their performances and productivity. Because there is a wide range of different mycotoxins, with different chemical structures, a simple approach cannot efficiently solve the problem. Quality of raw materials, prevention of the occurrence of mycotoxins, control and testing systems are all essential to reducing the exposure of humans and animals to mycotoxin.

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