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## **Mycotoxins and animal health: A short note**

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#### **Abstract**

Dietary exposures to environmental food pollutants such as mycotoxins have gained enormous significance due to their adverse effects on production and reproduction in animal and human populations. The purpose of this review article is to summarize the most relevant and recent information available on mycotoxins. This includes information about their occurrence, toxicity, clinical signs, diagnosis, treatment and control as well as their significance in feed and food.

**Keywords:** mycotoxins, animal health, short note

#### **Introduction**

Mycotoxin are secondary metabolites produced by pathogenic micro fungi and they contaminate foods, feeds as well as their raw ingredients and around 25% of world's cereals are contaminated with known mycotoxins, thus posing a severe hazard to the human as well as animal health [6, 14, 10]. The Ideal temperature for growth of the pathogenic microfungi is 25-32 °C and Humidity- 90-95% [5]. Among the mycotoxins, the enormous studies and details have been done of aflatoxin B1 and ochratoxin A, but other mycotoxins such as citrinin (CIT) have not been done due consideration in spite of its harmful effects on reproduction as well as patho-physiological effects on the renal and other vital organs [6]. Citrinin and ochratoxin A show nephrotoxicity, and have carcinogenic as well as mutagenic properties and the toxicities of mycotoxins have usually been assessed using experimental animals [7]. The worldwide rye ergot (*Claviceps purpurea*) poisoning of livestock occurs due to ergot alkaloids (e.g., the vasoconstrictor, ergotamine and the uterotonic, ergometrine) act as dopamine, serotonin and noradrenaline antagonists, generate a cascade of physiological effects, including diminished peripheral blood circulation as well as decreased prolactin concentration in circulation. Some of the more visible consequences comprise make worse against heat stress response, severe reduction in milk yield, and gangrene of extremities in cold environment [27, 28, 29]. The consumption of Kodo millet is often reported to cause intoxication and poisoning especially in north India. The millet is toxic to animals as well as humans due to it is often found heavily infested with *Aspergillus tamari* lead to Isolated Fumigaclavin A and cyclopiazonic acid toxicity [24]. The toxicities of mycotoxins have generally been measured using experimental animals. Since the MDCK cell line was established from kidney cells, it may be a suitable model for analyzing the nephrotoxicities of citrinin and ochratoxin A. MDCK cells were more susceptible to ochratoxin A than to citrinin [7]. The conformatory diagnosis is examination of feed in laboratory. This article reviews the classification, sources, some possible etio-pathogenesis, clinical signs, diagnosis as well as the major strategies of treatment and control in affected animals.

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**Table 1:** Etiopathogenesis, clinical sign, diagnosis and their treatment and control of Mycotoxin

Mycotoxins	Source	Affected animals	Pathogenicity actions	Clinical signs	Diagnosis	Treatment & Control
Aflatoxin [1, 2, 4, 5, 10, 25, 26] B1>G1>B2>G2 Second generation metabolites M1 and M2	<i>Aspergillus flavus</i> , <i>A. parasiticus</i> , <i>Penicillium puberulum</i> ,	LD50 Rabbit-0.3 0.5mg/kg Duck- 0.5mg/kg Chicken- 2mg/kg Cattle- ≥ 100µg/kg [Ducklings> rabbit> turkey, chicken> neonatal rat> cat, pig, cattle, sheep]	Carcinogenic, Hepatic necrosis, Nephrotoxic, immunosuppressive	Acute- weakness, anorexia, anaemia, epistaxis, petechiae on mucous membrane, bloody faeces, icterus, possible convulsion and death. Subacute: Jaundice, hematomas, hemorrhagic enteritis, moving on circles, ear twitching teeth grinding. Chronic: reduced feed conversion efficiency, productivity, weight gain and in poultry egg quality hampered	Acute: Increase ALT, AST, ALP, bilirubin, prothrombin time Chronic: hypoproteinemia, Aflatoxicosis M1 detected in milk	0.5% Hydrated Sodium calcium aluminosilicate as feed additive (5kg/tonn). Activated charcoal 6.7mg/kg, Intraruminally Low fat and high protein diet. Amoniation of feed, anticaking agent mix with feed and toxin binder hydrated sodium calcium aluminosilicate (HSCAS) in feed of poultry as well as pig (5kg/tonn) and sodium bentonite is used
Rubratoxins [3, 4, 5]- Rubratoxin A & B	<i>Penicillium rubrum</i> , <i>P. purpurogenum</i>	Poultry, Lab animals comparatively resistance, Oral LD50 for rats 400-500 mg/kg BW (vehicle is Dimethyl sulphoxide) It produces extensive haemorrhage through the body	It forms toxic metabolite due to presence of lactone ring bind with DNA and alter DNA polymerase activity. Disaggregation of ribosome inhibits the certain protein & enzyme Hepatotoxic, nephrotoxic, splenotoxic, Teratogenic, embryotoxic	Haemorrhagic syndrome in poultry, joundice, head pressing and ventral erythema in swine		
Ochratoxin [4, 5, 7, 8, 18, 19]	<i>Aspergillus ochraceus</i> <i>Penicillium viridicatum</i>	Pig, poultry, horse, cattle, sheep Acute toxic dose for Pig & Poultry : 1-5 ppm, Mice – 24ppm MDCK cell line - 2ppm [7]	Nephrotoxic, Carcinogenic [18] Ochratoxin inhibits anion transport and oxydative phasphorylation in PCT→ Release of brush border enzyme like leucine amine peptidase → Damage renal tubule→ decrease metabolic clearance and urine concentrating ability	Polyurea, Polydipsia, dehydration and severe anaemia followed by death. Reduced reproductive performance of swine. It is immunosuppressent and reduces sperm quality in Boar and also cause faetal death and abortion in sow		<i>Trichosporon mycotoxinivorans</i> (TRM) cleaves OTA into phenylanine and the non-toxic OTA metabolite. In dietary inclusion of TRM suppress the detrimental effects of OTA on the immune system of broiler chicks [19]
Citrinin [4, 5, 6, 7, 9, 10, 25]	<i>Aspergillus terreus</i> <i>Penicillium viridicatum</i> , <i>P. verrucosum</i> , <i>A. terreus</i>	Pig (highly sensitive), domestic birds. LD50 MDCK cell line -6ppm [7]	Primarily nephrotoxic, mild hepatotoxic	Pruritus, hair loss, papular dermatitis, unthriftyness, Reduced weight gain, decreased feed conversion efficiency		
Ergotoxin [4, 5, 12, 13, 14, 25] ergotamine, ergotometrine, erocornine, ergocristine, ergosine	<i>Claviceps purpurea</i>	At 200-600 ppb ergot alkaloid produce clinical sign in Cattle, pig, sheep, horse, poultry Acute : common in carnivores, horse and sheep and rare in cattle Chronic: Cattle (most common)	Acute: Neurotoxic, Indoles and Lysergic acid derivatives lead to interference of brain neurotransmitters. Chronic: gangreenous, vasoconstriction, oxytotics and dry gangreene formation due to thrombosis.  Dopamine agonism, 5-HT agonism, pituitary Prolactin antagoism,	Acute: weakness, recumbency, epidemic hyperthermia (105-107 F), dyspnoea, hypersalivation ataxia, tremors, staggering gait, posterior paralysis, intermittent blindness and death may due to anoxia during convulsion. Chronic: lamness, swelling of fetock and pastern joint, sloughing of hoof and tail, affected parts has cold and loss of sensation.	Gangreen on ther extrimities, necropsy finding ulceration of oral, pharyngeal and ruminal mucosa in sheep.	→Saline purgative (magnesium sulphate @ 1g/kg, PO), →Convulsion, tremor, and behavioural abbration treated with diazepam. →Necrotic lesion treated with antibacterial and fly repalants ointment →Anticholinergic drg Physostigmine acts as a vasodilator in extrimities can preventing from necrosis →Dopaminergic agonist, domperidone@ 1.1mg/kg, PO, BID for 14 days

						preventing agalactia.
Patulin [4, 20, 21, 25]	<i>Penicillium patulum (P. urticae), P. expansum</i>	Cattle, piglets, chicks and mice LD50 in chicks: 170mg/kg	Patulin is an electrophilic molecule that exerts its deleterious effects by binding covalently to cellular sulfhydryl (SH, thiol) groups of proteins and glutathione. Neurotoxic, increase spontaneous release of lutamate and aspartate. reproductive and developmental toxicity, carcinogenicity, mutagenecity and immunotoxicity	“Rye grass staggers” characterized by ataxia and convulsion in cattle, pedalling of limbs in calves, tetanic convulsions, opisthotonus, nystagmus and profuse salivation. Haemorrhagic gastroenteritis in rats. In ruminants, it has an antibiotic effect on rumen bacteria. In cattle and sheep, it develop brain haemorrhages, pulmonary edema, abomasum and hepatorenal haemorrhage		Magnesium sulphate, Diazepam. Reducing agents like sulfhydryl (SH, thiol) containing agents and Ascorbic acid lead to inactivate patulin
Citreoviridine (Yellow Rice Toxin) [4, 10]	<i>Penicillium citreoviride</i>		Neurotoxic, respiratory paralysis and cardiac failure	Palpation, nausea, vomiting, cold and cyanotic extrimities, hypotension, convulsion and death due to cardiac and respiratory failure.		
Zearalenone [4,5, 10, 22] $\alpha$ and $\beta$	<i>Fusarium graminearum F. roseum</i>	Pig (1-3ppm) Cattle (> 10ppm), Sow and cow : 3.6mg/kg	Estrogenic $\alpha$ zearalenone is 3-10 times more potent than $\beta$ zearalenone. $\alpha$ zearalenone is major metabolite in pigs and $\beta$ zearalenone is major metabolites in cattle. $\alpha$ zearulene binds with E <sub>2</sub> receptor present in uterus → $\alpha$ zearulene - E <sub>2</sub> receptor complex → this complex is translocated to nucleus and induces the synthesis of DNA polymerase I & DNA polymerase II → Synthesis of nucleic acid and protein → increased water permeability of uterus → increased permeability of uterus to glucose, protein, RNA Beside this F2 toxin binds with E <sub>2</sub> receptor present in pitutary gland & hypothalamus → persistance over stimulation → prolonged estrous cycle, ovarian atrophy and enlarged mammary gland	Porcine vulvovaginitis and hyperestrogenic syndrome in pig, reduced conception, nymphomania and repeat breeding in cow, Preputial prolapse and retardation of gonadal development in bulls, urethral obstruction,		Administration of 10mg PGF-2 $\alpha$ parenterally, Activated charcoal orally, dehydrated alfa alfa feed (15% in ration or feed).
Sporidesmin [4, 5, 22]	<i>Pithomyces chartarum (Sporidesmium bakeri)</i>	Cattle, sheep, deer	Hepato-biliarytoxic, inflammation of the bile ducts and progressive obliterative cholangiolitis photosensitization, injury to tissues of the urinary bladder and mammary gland	Facial eczema in cattle, joundice, secondary photosensitive dermatitis. lethargy, dullness, anorexia,		Hepatotonics,antibacterials, antihistaminics and administration of very high doses of zinc (15–30mg /kg BW/day) to sheep and cattle as either zinc oxide by drenching fungicides used to control the growth of <i>P. chartarum</i> , carbendazim was best (at 0.15 and at 0.30 kg/hectare of active ingredient), while benomyl and

						thiophanate methyl was effective only at 0.30 kg/hectare fungistatic agents to pasture included thiabendazole or benomyl (Benlate) sprayed on at the rate of 272 g/hectare
Trichothecenes (T2 toxin)/ Fusariotoxicosis [4, 5, 14, 23]	<i>Fusarium sporotrichoides</i> , <i>F. roseum</i> , <i>F. tricinctum</i>	Cat (most sensitive), Buffalow Acute oral LD50 for T2 toxin Rat : 3.8 mg/kg Day old chick: 5 mg/kg Swine : 4 mg/kg	Protein synthesis inhibitor, radiomimetic effect, lipid peroxidation, immunosuppressant, irritants	Acute: haemorrhagic gastro-enteritis, tachycardia, tachpnoea, posterior weakness, haematuria, unthriftiness, death due to hypotension and shock. Chronic: spreading bright red or dark cherry red petecheal rashes on the skin, ulceration and gangreen formation on larynx. Degnala disease (gangrenous syndrome) In water buffaloes which is characterise by necrosis and swelling of the tips of the ear, tail, tongue and subsequent sloughin of the skin lead to formation of open wounds		Activated charcoal, magnesium sulphate, dexamethasone, sodium bicarbonate, metaclopramide.
Fescue toxicosis [5, 15, 16, 17, 22, 25, 26]	<i>Festuca arundinacea</i> <i>Neotyphodium coenophialum</i> , <i>Neotyphodium lolii</i>	Prgnant mares (highly susceptible), Cattle, sheep  Ergovalin concentrate > 200ppb toxic for horse, cattle & sheep	Decerases prolactin and progesteron level, <i>Neotyphodium lolii</i> produces 3 major groups of toxins: Tremorgenic indole diterpenoids such as paxilline and lolitrem B, ergopeptide alkaloids such as ergovaline, an insect herbivory repellent compound, peramine  Thiamine increased feed intake during hyperthermia that lead to increased pathogenesis. Ergovalin: Dopamin agonist, prolactin inhibitor.	Alters grazing behavior and performance of ruminants. "Summer fescue toxicosis" occurs mostly in summer season which characterised by thickened placenta, Abortion, still birth, agalactia in horse and cattle. "Fescue foot" and fat necrosis in cattle. Photosensitization, hyper salivation, rough hair coats, tachypnoea and hyperthermia with reduced body-weight gains in cattle. "fescue foot" in cattle and sheep occurs in winter which is characterised by gangrenous necrosis and sloughing of the affected hoof. Temperature entolerance, epidemic hyperthermia, erythema and swelling on coronary, paddling and weight shifting.		→Treatment of parental plants with fungicide →Thiabendazole 5g/45.5kg BW repeat every 7 days. →Ammonication of affected hay. → <b>Summer fescue toxicosis</b> is terated with Domperidone@1.1mg/kg,PO, BID for 10-14 days →Glucmannans is a Yeast cell derivatives preventing toxin absorption on cattle.
Fumonisin [14, 25] fumonisin B1, B2, B3, B4, A1 and A2	<i>F. verticillioides</i>	Horse, pig, poultry, monkey → Horse and pig (most sensitive) than cattle and poultry	Carcinogenicity, Hepatotoxicity, → block the synthesis of sphingolipids leading to the intracellular accumulation of sphingosine and sphinganine and coagulation necrosis of cells in sensitive organs, especially the brain, heart, liver, and kidney	Equine leucoencephalomalacia (ELEM) in horses when fumonisin B1 ≥10ppm, porcine pulmonary oedema and hydrothorax syndrome (PPE) in pigs, Hepatotoxicity and atherosclerosis in monkeys, immunosuppression in poultry. transient abdominal pain, borborygmus, diarrhoea and patient fully recovered after some times. ELEM have Neurotoxic syndrome the signs are initial anorexia, lethargy, and absence of	Sphinganine and sphingosine are excreted in the urine and serum and this is used as a biological marker of exposure to fumonisins.	

				<p>gastrointestinal sounds, then hypersensitivity and agitation, sweating, muscle tremor and weakness, hypermetria, staggering, Circling, inability to swallow, lower lip paralysis, protusion of a flaccid tongue, apparent blindness, absent menace reflex, pupillary dilation, absent pupillary light reflex, circling, head pressing, collapse, and tonic-clonic convulsions</p> <p>Hepatotoxic syndrome signs are edematous swelling of the lips, nose, supraorbital fossa, and lower limbs. Jaundice, cyanosis, mucosal petechiae, and dyspnea are common signs. Death occurs after a course of 48-72 hours. Many horses are found dead without signs having been observed.</p>		
<p>Kodo poisoning / Cyclopiazonic acid [10, 24, 25]</p>	<p><i>Penicillium cyclopium</i>, <i>Penicillium camembertii</i>, <i>Aspergillus versicolor</i>, <i>Aspergillus oryzae</i>, <i>Aspergillus flavus</i></p>	<p>Rats, chickens, dogs →Humans as well as animals, →severe hepatic lesions and cell necrosis in rats at 50 mg/kg body weight orally</p>	<p>Neurotoxic, nephrotoxic, hepatotoxicity Acute hepatotoxicity: Marked increase in the activity of Serum glutamate pyruvate transaminase (SGPT) and Serum glutamate oxaloacetate transaminase (SGOT). Hepatocarcinogenicity: Significant increase was also observed in gamma glutamyl transpeptidase (GGT) activity following CPA exposures, indicating preneoplastic changes in the rat liver.</p>	<p>→In rats, focal necrosis in many organs. →In chickens, caused reduced weight gain and produced proventricular lesions →In dogs lesions were gastrointestinal tract and kidneys →Diarrhoea and vomition in non-ruminant animals</p>	<p>Necropsy lesion: gastric ulcer, haemorrhage and Hepatocellular necrosis</p>	
<p>Slaframine [25]</p>	<p><i>Rhizoctonia leguminicola</i></p>	<p>cattle, goats, and horses</p>		<p>'Slobbers syndrome', in cattle, goats, and horses. Which is characterized by profuse salivation Excessive lacrimation, stiff gait, tremor, frequent urination, dyspnea, bloat, anorexia, and diarrhea also occur.</p>		

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