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CHAPTER 14

Study of Ochratoxin and Ochratoxicosis

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Abstract

The incidence of ochratoxicosis in India, while not extensively documented, has been a concern due to the country's agricultural practices and climate, which can promote the growth of ochratoxin-producing molds. Food Contamination: Various studies have indicated that foods commonly consumed in India, such as cereals, pulses, and dried fruits, can be contaminated with ochratoxin A (OTA). Factors like poor storage conditions, humidity, and inadequate pest control contribute to this contamination. Health Studies: Research has shown the presence of ochratoxins in food products in different regions of India. However, comprehensive epidemiological studies specifically linking ochratoxicosis to health outcomes in the Indian population are limited. Public Health Impact: The potential health risks associated with ochratoxin exposure, including kidney damage and cancer, highlight the need for monitoring and regulation. Some studies have pointed to correlations between ochratoxin exposure and health issues, but further research is needed to establish clear incidence rates. Regulatory Measures: Indian authorities,

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along with international agencies, are increasingly focusing on mycotoxin regulations and monitoring to improve food safety.

Keywords: Mycotoxin, Ochratoxin, Ochratoxicosis

Introduction

Mycotoxins

Mycotoxins are toxic compounds produced by certain molds (fungi) that can contaminate food and feed (Verma *et, al.*,1994). They pose significant health risks to humans and animals when ingested, inhaled, or absorbed through the skin. Mycotoxins are

a) Aflatoxins: Produced by Aspergillus species, commonly found in grains, nuts, and seeds. They are potent carcinogens.
b) Ochratoxins: Produced by Aspergillus and Penicillium, often found in cereals, coffee, and dried fruits. Ochratoxin A is the most toxic.
c) Fusarium Toxins: Includes zearalenone and deoxynivalenol (DON), commonly found in grains like wheat and corn.
d) Patulin: Found in fruits, especially apples, and produced by molds like Penicillium.

Ochratoxin

Ochratoxins are the low molecular weight substances and are produced by fungus of *Aspergillus* and *Pencillium*. *viz., Aspergillus alliaceus, Aspergillus. melleus, Aspergillus stiamus, Aspergillus. pertakii, Aspergillus. Sclerotiorum, Aspergillus. sulphureus* (Hesseltine *et al.*, 1972) and *Pencillium. commune, Pencillium. cyclopium, Pencillium. variable, Pencillium. purpurescens and Pencillium. palitans* are produce ochratoxin (Scott *et al.*, 1970). Chu (1974) considered A. Ochraceus as the principal producer of ochratoxin A. Hamilton *et al.* (1982) and Dwivedi and Burns (1984) indicated *Aspergillus ochraceus* and *Penicillium viridicatum* as the principal producer of ochratoxin.

Ochratoxins are crystalline, colorless substances that glow blue when exposed to ultraviolet light. The sodium salt of ochratoxin A is soluble in water; as an acid, it is moderately soluble in polar organic solvents (e.g. chloroform and methanol). The following table provides a summary of some of the main ochratoxins chemical and physical characteristics.

Table 1: Ochratoxin's chemical and physical characteristics

Ochratoxin	Molecular Formula	Relative molecular mass	Melting point (˚C)	Absorption Absorption	Maxima (nm) Co-efficient (€)	Reference
A(OTA)	C_{20} H_{18} $ClNO_6$	403	169 (xylene)	213 (36800)	322 (6400)	Steyn and Holzapfel (1967)
B(OTB)	C_{20} H_{19} NO_2	369	89-95 (benzene)	218 (37200)	318 (6900)	Vander Merwe et al. (1965)
C(OTC)	C_{ll} H_9 ClO_5	256	221-229	212 (30000)	338 (5600)	Vander Merwe et al. (1965)

Incidence of Ochratoxins

When it was first recognized, it was thought to be a component of storage flora that included poor post-harvest storage conditions and unfavorable conditions throughout the distribution of goods like peanuts. Toxigenic Aspergillus ochraceus and Penicillium viridicatum are storage fungi (molds) that create ochratoxins, a class of mycotoxins, when exposed to high moisture content and ideal temperatures. Even though reports of ochratoxin's natural presence in agricultural goods have come from all over the world and on a wide variety of crops, the amounts of ochratoxin found differ significantly from place to place. Generally speaking, goods from tropical and sub-tropical nations, where the climate is favorable for the growth of mold and the manufacturing of toxins, include higher levels of toxins. North American grains have been found to contain ochratoxin, albeit in trace amounts (Shotwell *et al.*, 1969). Even at low moisture content, Buckle (1983) discovered ochratoxin A in 12.8% of cereals; substantial quantities of ochratoxin A were observed in barley and wheat in particular. According to Krogh (1978), up to 14% of grains were contaminated with ochratoxin A. Ochratoxin A concentrations in coconut samples ranged from 50 to 205 mg/kg, according to Zohri and Saber (1993). Skrinjar *et al.* (1992) reported ochratoxin A and ochratoxigenic molds in forages and grain feeds, whereas Hald *et al.* (1993) reported ochratoxin A in wheat. In India, ochratoxin A has been found in Tamil Nadu sorghum (Manickam *et al.*, 1985) and Andhra Pradesh broken rice (Reddy *et al.,* 1983). Ochratoxin A has been found to be present in bread up to 80 ppm (Visconti and Bottalico, 1983) and retail flour up to 6.5 ppm (Osborne, 1980). The public's health is seriously threatened by the natural presence of ochratoxins in cereals, coffee, beans, feed, animal products, processed foods, and beer (Krogh *et al.*, 1976; Cooper *et al.*, 1982; Petkova-Bocharova and Castegnaro., 1985).

Ochratoxicosis

Ochratoxicosis refers to the toxic effects resulting from exposure to ochratoxins, particularly ochratoxin A (OTA). This condition can occur in both humans and animals and is primarily linked to the consumption of contaminated food products.

Van Der Merwe *et al.* (1965) were the first to report ochratoxicosis as a toxic metabolite of Aspergillus ochraceus; nevertheless, it was not until OA was isolated from the sorghum seed strain K-804 in South Africa that its full poisonous potential was recognized (Scott, 1965).

Ochratoxin A was originally discovered naturally contaminated in a corn sample by Shotwell *et al.* (1969). Later, Ochratoxin A was also isolated from peanuts (Doupnik and Peckham, 1970), cereals, and sorghum (Scott, 1965; Scott *et al.*, 1972), as well as stored grains (Christensen and Kaufmann, 1969). Penicillium viridactum has also been isolated from barley (Buckle, 1983), wheat (Scott *et al.*, 1972), and corn (Krogh and Hasselagar, 1968). It should be mentioned that Aspergillus alutaceus is the new name for A. ochraceus. Huff *et al.*, (1974) opined that ochratoxicosis caused great threat to both human and animal health. Further, Huff *et al.*, (1975) indicated that ochratoxin has structurally related secondary metabolites designated as ochratoxin A, B and C of which ochratoxin A (OA) is extremely toxic.

Hamilton *et al.* (1982) documented naturally occurring epidemics of ochratoxicosis in poultry and examined five separate cases of the disease in turkeys, two cases in layers, and two cases in broiler chickens in the United States. After screening 50 samples of maize from several feed manufacturers in and around Hyderabad, Devi and Polasa (1982) found that six of them had ochratoxin.

Ochratoxin was found in a variety of grains, cereals, plant products, animal feeds, and meat from various nations, according to Krogh (1987) and Marquardt *et al.* (1988). Ochratoxin was found in feed samples from various chicken farms in Punjab, according to Gaur *et al.* (1991). Nine of the 42 poultry feed samples examined by Raina and Singh (1991) were positive for ochratoxin.

According to Egmond and Spijers (1994), ochratoxin contamination was more common in cereals and animal meat products, with levels ranging from 10 to 500 µg/kg in various ingredients. In the Namakkal region of Tamilnadu, Chandrasekaran (1996) observed elevated levels of ochratoxin A in layer mash (5.6%) and sunflower oil cake (37.0%).

Devegowda *et al.* (1998) examined ochratoxin A in a variety of feed ingredients gathered from around India and found that the toxin concentration varied from 10 to 300 ppb, with an overall incidence of 34.5%. When comparing oilseed and oilseed meals to maize byproducts, a higher frequency of 57% was noted.

When Thirumala Devi *et al.* (2002) evaluated 216 items that were supposed to be added to chicken meals between 1998 and 2001, they found that 6% of the samples had ochratoxin contamination. The ochratoxin Nine out of 29 sorghum, one out of 27 groundnut, one out of 14 rice bran, one out of ten sunflower, and two out of eight millet samples had contamination levels greater than 10 µg/kg. Corn, soybeans, and mixed feeds did not contain ochratoxin.

Pathological Symptoms

In pigs and poultry, ochratoxicosis is a prevalent natural occurrence. With contaminated feed containing ochratoxin A in quantities ranging from 2 to 16 ppm, Hamilton and his colleagues (1982) reported the first verified naturally occurring epidemic of ochratoxicosis in turkeys, laying hens, and broilers, resulting in 21–59% mortality. In addition, Bodnarchu and Kaspruk (1984) reported a 42%

fatality rate from an ochratoxicosis outbreak in ducks. Chicks, dogs, and rabbits fed naturally infected moldy bread with 80 ppm of ochratoxin A and 9.6 ppm of ochratoxin B have been shown to develop a fatal gastroenteritis (Visconti and Botalico, 1983). Adult cattle's rumen content has been shown to inactivate ochratoxin A in vitro (Hult *et al.,* 1976). However, weaned calves have been shown to be vulnerable to ochratoxin A toxicity at dietary feed levels ranging from 2 to 40 ppm (Pier *et al.,* 1976). Many experimental animals have been used to study the toxic effects of ochratoxin A (Marquardt and Frohlich, 1992; Madyastha *et al.,* 1990). Every animal that has been examined thus far has been shown to be vulnerable to ochratoxin A. Fish, birds, and mammals are among the ten test animal species in which experimental ochratoxicosis (nephropathy) has been induced.

In Denmark, porcine mycotoxic nephropathy has long been well-documented. The constant presence of ochratoxin A (2 to 70 pg/Kg) in the feed and the frequent presence of the mycotoxin in the kidneys of killed animals (2 to 70 µg/kg) are the primary causes of pig nephropathy. Degeneration of the proximal tubules, atrophy of the tubular epithelium, interstitial fibrosis in the renal cortex, and hyalinization of certain glomeruli were observed upon inspection of the sick kidney. Experimental animals given meals containing ochratoxin levels have replicated the typical illness symptoms observed in field cases of mycotoxic porcine nephropathy. This disease is typically linked to natural outbreaks While hens and chickens fed 300–1000 µg/kg of ochratoxin A for a year developed avian nephropathy, pigs fed rations containing 200–4000 µg/kg of ochratoxin A exhibited nephropathy signs over the course of several months (Krogh *et al.,* 1976b).

In 1957 and 1958, it was discovered that up to 75% of the households in a number of valley floor villages in the neighboring countries of Yugoslovia, Romania, and Bulgaria suffered from chronic nephropathy, also known as Balken endemic nephropathy. Krogh and his colleagues provided evidence that individuals in this endemic area ingest larger quantities of ochratoxin A more frequently than those in areas devoid of nephropathy, despite the fact that genetic variables seem to play a role. In addition, a remarkably similar nephropathy was identified in slaughtered pigs in Denmark (Krogh *et al.*, 1976 b).

In one study, 639 sera from residents of two villages in Yugoslovia a region where endemic nephropathy is common were tested for ochratoxin A, and 6.6% of the samples tested positive. Ochratoxin A concentrations varied between 2 and 57 ng/l (Huff *et al.,* 1983). Furthermore, papillomas and carcinomas of the renal pelvis, ureter, or bladder were found in approximately one-third of patients who died from Balken endemic nephropathy (BEN) (Castegnaro and Chernozemsky, 1987).

According to Di Paolo *et al.* (1993), breathing in Aspergillus ochraceus ochratoxin can cause acute renal failure (ARF). A farmer and his wife experienced brief respiratory discomfort after eight hours in a granary that had been shuttered for several months. The woman then experienced nonoliguric acute renal failure twenty-four hours later, and a biopsy confirmed tuberculosis, which resolved in twenty-four days. Although no toxic compounds were discovered, Aspergillus ochraceus strains that produce ochratoxin were identified from the wheat.

Ochratoxin A was identified by Breitholtz and his colleagues (1993) in milk that had undergone a liquid-liquid extraction process and purified on a silica-gel column contained in a Pasteur pipet. Ion-pair

liquid chromatography with fluorescence detection was used to evaluate the purified samples. To determine the amount of ochratoxin A in cow's milk, the detection and quantification limits were 10 and 40 ng ochratoxin A/L milk, respectively. The examination of human milk was subject to the same limitations. In another investigation, 40 human milk samples and 3b cow milk samples that were gathered in Sweden were examined. Five (14%) of the cows' milk samples contained ochratoxin A (range 10-40 ng/L). The mothers who provided milk samples also had their blood drawn. 39 samples in all were examined. Ochratoxin A was present in all blood samples in amounts higher than the quantification limit of 60 ng/L blood. The average amount of ochratoxin A in human milk was less than or equal to 0.1 times that of human blood.

Clinical Signs in Ochratoxicosis

Clinical indications of listlessness, huddling, diarrhea, tremors, and prostration were recorded by Huff *et al.* (1974) 22 to 25 hours after a single oral dose of 16 mg OA per kg diet. According to Huff *et al.* (1975), the main clinical indicators of ochratoxicosis in broiler chickens in field conditions were poor development, increased feed consumption, and increased moisture content in feces. During acute short-term toxicity testing with OA in broilers, Galtier *et al.* (1980) noted huddling, hypothermia, cachexia, tremors, ptosis, diarrhea, and a decrease in spontaneous activity. Broiler ochratoxicosis has also been linked to lower bone strength, anemia, and feed consumption.

In birds fed 1.0 ppm of ochratoxin, Pier *et al.* (1980) noted emaciation, diarrhea, pale comb and wattles, and decreased water consumption. In contrast, Hamilton *et al.* (1982) noted reduced feed intake, subsequent air sacculitis, and mortality in both natural and experimental ochratoxicosis instances.

Depressed growth, dullness, huddling, decreased appetite, lower feed intake, frailty, and diarrhea were all recorded by Dwivedi and Burns (1984) in broilers given 2 and 4 ppm of OA.

According to Raina and Singh (1991), broiler chicks fed a diet containing 1.0 ppm of ochratoxin experienced general symptoms such as dullness, inappetance, decreased feed intake, and occasionally anemia. The main symptoms of experimental ochratoxicosis in broilers were anorexia, unthriftiness, droopy wings, ruffled feathers, a chilly appearance, a neck tucked into the thoracic cavity, and yellowish diarrhea (Thyagarajan *et al.*, 1996).

Clinical indications of experimental ochratoxicosis in broiler chickens included dullness, ruffled feathers, huddling inappetance, diarrhea, polydypsia, poor feed conversion, and stunted growth (Amita, 2001). In birds administered 1.0 ppm ochratoxin for five weeks, Bhanuprakash (2002) observed dryness, depression, ruffled feathers, listlessness, huddling, decreased feed consumption, stunted growth, and white pasty diarrhea.

Metabolism

Galtier (1974) discovered that the stomach wall had the highest tissue level of unaltered ochratoxin A in the first four hours after a single dose of the drug (10 mg/kg body weight) given by gavage to rats. Small levels of unaltered ochratoxin A were found in the caecum, small and large intestines, and both. Furthermore, trace levels of the isocoumarine moiety (ochratoxin α) (1–3% of the overall dose) were also found in the large intestine and caecum. Rats intraperitoneally injected with ochratoxin A have been shown to have ochratoxin an in their urine and feces (Galtier, 1974), suggesting that ochratoxin A cleaves into ochratoxin a and phenylalanine in these circumstances. By using the HPLC method, Valenta *et al.* (1993) found ochratoxin A in pig pee and feces. Research using 14c-labeled ochratoxin A revealed that the body produces other, as-yet-unidentified metabolites. Within 24 hours of receiving a single intraperitoneal injection of [c 1 phenylalanine, which was recognized as ochratoxin A, less than half of the radioactivity was eliminated in the urine (Chang and Chu, 1977).

When albino and brown rats were given ochratoxin A intraperitoneally or orally, 1–1.5 percent of the dose was eliminated in the urine as (4 R) 4 hydroxy ochratoxin A, and 25–27% as ochratoxin α (Storen *et al.*, 1982). Both (4s) and (4R) - 4 hydroxy ochratoxin A were generated in vitro utilizing liver microsomes from pigs, humans, rats, and rabbits through a hydroxylation process involving cytochrome p-450 (Stormer and Pedersen, 1980; Stormer *et al.*, 1983). Up to 40 mg/kg body weight of 4-hydroxy-ochratoxin A is non-toxic to rats (Hutchison *et al.*, 1981). Thus, it was determined that the microsomal hydroxylation probably signifies a detoxifying process. According to Roth *et al.* (1993), ochratoxin A prevents Bacillus subtilis from growing. In vitro research have demonstrated that ochratoxin A binds to serum albumin (Chu, 1971; 1974). In vivo experiments in rats have also noted similar binding (Galtier, 1974).

Acute and Chronic Effects

Ochratoxin A can cause acute poisoning in a variety of species, with LD50 values ranging from 3.4 to 30.3 mg/kg. The female rats were found to be more sensitive than the males when ochratoxin A was given to them orally. Studies on acute effects have also observed changes in the liver, despite the fact that the kidney is the target organ (Galtier, 1974; Krogh, 1976). In addition to renal lesions, additional renal effects involving the liver, gut, spleen, lymphoid tissue, and leucocytes were noted in pigs and dogs at large oral dosages, which corresponded to feed levels exceeding 5–10 mg/kg (Szczech *et al.*, 1973 a, b, c).

Clinical signs included polyuria, elevated glutamate oxalo acetate transaminase (GOT) activity in serum, and mild enteritis in calves fed ochratoxin A-containing rations at 0.1 to 2 mg/kg body weight for 30 days (Pier *et al.*, 1977). There was minimal tubular deterioration in the kidney. Chicken exposed to elevated levels of ochratoxin A showed signs of acute necrosis and "vlueral goat" (Peckham *et al.*, 1971). When ochratoxin A was administered orally to rats along with either biscoumacelate or phenylbutazone, the toxin's LD50 values and pathological alterations increased. This was likely due to the toxin's displacement from binding sites on plasma proteins (Galtier *et al.*, 1980). In vitro experiments showed that ochratoxin A had harmful effects on the monkey's renal epithelial cells, manifested as aberrant mitotic cells (Steyn *et al.* 1975). A dose-related decrease in thymic mass and myelotoxicity, defined by bone

marrow hypocellularity, decreased marrow pluripotent stem cells, and granulocyte-macrophage progenitors were noted in mice given a total dose of ochratoxin A up to 8 mg/kg over an 8-day period (Boorman *et al.*, 1984). Serum immunoglobulin concentrations were found to be 57–66% lower than normal in a group of chicks fed ochratoxin A at a dosage of 0.214 ppm for 20 days (Dwivedi and Burns, 1984). When given orally to albino Swiss mice for 14 consecutive days, ochratoxin (1 pg/kg b.w/day) enhanced the incidence of chromosomal aberrations in mitotic and meiotic metaphase, according to Kumari and Sinha (1994).

Teratogenicity

When ochratoxin A (5 mg/kg body weight) was injected intraperitoneally into pregnant mice on one of the gestation days between 7 and 12, the result was a decrease in foetal weight, an increase in prenatal mortality, and a variety of foetal malformations, such as exencephaly and abnormalities of the eyes, face, digits, and tail (Hayes *et al.*, 1974). Another study found that most foetuses from dams treated on days 15–17 developed cerebral necrosis after receiving 3-5 mg/kg body weight of ochratoxin A intraperitoneally or orally on gestation days 8, 9, 10, 15, 16, and 17. In contrast, no cerebral necrosis developed after treatment on days 8–10, when ochratoxin A is overtly teratogenic (Szczeck and Hood, 1981). Mice, rat, and hamsters are all teratogenic to ochratoxin A (Shirai *et al.*, 1985). Foetuses taken on day 20 of gestation displayed reduced weight and a number of malformations when rats were given oral ochratoxin A at 0.75 and 1.0 mg/kg body weight on days 6–15 of pregnancy (Brown *et al.*, 1976). On the eighth day of pregnancy, rats fed ochratoxin A orally at a dose of 5 mg/kg body weight showed lower development and fewer litters (More and Galtier, 1975). The greatest number of abnormalities, such as hydrocephaly, omphalocele and amophthalmia, and a shift in the position of the oesophagus, were shown in rats given ochratoxin A subcutaneously (1.75 mg/kg body weight) on gestation days 5-7 (Mayura *et al.*, 1985). While higher doses (5 mg/kg body weight) caused all fetuses to be absorbed, smaller doses (0.5 and 1 mg/kg body weight) had no teratogenic effects.

Increased prenatal mortality and birth abnormalities, such as hydrocephalus, micrognathia, and heart problems, were noted in hamsters given intraperitoneal injections of ochratoxin A at dosages of 5–20 mg/kg body weight on one of the gestation days 7-9 (Hood *et al.*, 1976). It is known that giving mice ochratoxin A for one to two days can kill cells in the developing embryonic brain. Microcephaly was frequently observed. A dendritic expansion appears to be the cause of the deficiencies in synapse to neuron ratios observed in ochratoxin A-induced microcephalic brain (Fuki *et al.*, 1992).

Carcinogenesis

Kanizawa and Suzuki (1978) were reported a study which indicates that ochratoxin A is a hepatic and renal carcinogen in male mice. A group of 10 male mice were fed with a diet containing 40 mg ochratoxin A /kg for 44 weeks. Similarly, a group of 10 untreated controls were fed on the basal diet. All survivors were killed after 45 weeks. Hepatic cell tumours were found in 5 out of 9 treated mice and in none out of 10 controls. Solid renal cell tumors were found in 2 out of 9 treated mice and in none out of 10 controls. Cystic renal adenomas were found in 2 out of 9 treated mice and in none out of 10 controls. In another study, two groups of 50 male and 50 female B, C3 F, mice were fed on diet containing ochratoxin

A at 1 and 40 mg/kg feed respectively; one group (control) was fed on the basal diet. All survivors were killed after 24 months. Eleven out of 49 male mice in the 40 mg/kg group had renal carcinomas, 24 out of 49 male mice in the 40 mg/kg group recorded renal adenomas. All male mice in the 40 mg/kg group had microscopic evidence of nephropathy. A few females in the 40 mg/kg group had nephropathy changes, but no carcinomas or adenomas. Compound related lesions were absent in the control and the 1 mg/kg groups (Bendele *et al.*,1985).

The Japanese team then conducted a trial in which groups of 16 male mice were given a meal containing ochratoxin A at a rate of 50 mg/kg feed for several durations, ranging from 0 to 30 weeks (Kanizawa, 1984). After being exposed to ochratoxin A for 15 weeks, 3 out of 15 animals developed renal cell tumors; after 20 weeks, 2 out of 14 mice developed renal cell tumors and 2 developed hepatoma; after 25 weeks, 2 out of 15 mice developed renal cell tumors and 5 developed hepatoma; and after 30 weeks, 4 out of 17 mice developed renal cell tumors and 6 developed hepatoma. The control group did not exhibit these tumors. Bendele *et al.*, (1985), on the basis of their studies on ochratoxin A carcinogenesis in 57 BL/GJ X C_3 HF_1, mice, concluded that ochratoxin A is a renal carcinogen in male mice and a hepatic carcinogen in female mice. This study suggests that ochratoxin A is a potential carcinogen.

Ochratoxin A is a potent carcinogen in rats and has numerous other negative effects in animals, according to Marquardt's recent research and developments in Frohlich's (1992) understanding of ochratoxicosis. According to Bach *et al.* (1992), ochratoxin A is not thought to be a powerful carcinogen and only causes renal paranchymal cancer in male mice. Following oral treatment of 2.5 mg/kg of ochratoxin A to mice, the 32-p post-labelling method was used to assess the development and disappearance of ochratoxin A-DNA adducts in order to better understand the genotoxic effect of ochratoxin A (Pfohl-Leszkowiez *et al.*, 1993). Twenty-four hours after ochratoxin A was administered, a number of changed nucleotides were clearly seen in the DNA of the kidney, liver, and spleen; however, over the course of 16 days, their levels fluctuated considerably depending on the tissue and time. The kidney is the primary site of ochratoxin A's genotoxicity and most likely carcinogenicity, as evidenced by the fact that total DNA adducts peaked at 48 hours, with 103, 42, and 22 adducts per 10' nucleotides detected in the kidney, liver, and spleen, respectively. The liver and kidney had different main adducts. While some adducts remained in the kidney for as least 16 days following compound treatment, all adducts vanished in the liver and spleen by 5 days.

Immunotoxicity

An overview of ochratoxin A's effects on poultry immunological responses was provided by Burns and Dwivedi (1986). In a groundbreaking investigation, Richard *et al.* (1975) found that ochratoxin A considerably reduced the quantity of β globulin in the serum but had no effect on complement activity or antibody response to the Brucella abortus antigen in guinea pigs. Similarly, when Friesian calves were fed ochratoxin A and aflatoxin B_1, Patterson *et al.* (1981) found no discernible change in the levels of serum IgA, IgM, IgG_1, and IgG_2.

Haubeck et al. (1981) regarded ochratoxin A as a strong immunosuppressive agent based on a 50% decrease in IgM levels against sheep RBC in mice caused by low doses of the drug. Later, Creppy *et*

al. (1982) demonstrated that ochratoxin A also inhibited the IgG response in mice in a dose-related manner. Nevertheless, Prior and Sisodia (1982) reported contradictory results, failing to detect any changes in serum immunoglobulins in mice administered ocharatoxin A orally or intraperitoneally. However, intra-peritoneal treatment of ochratoxin A resulted in a considerable decrease in antibody titres to deceased B. abortus, even if oral administration of the drug did not. They hypothesized that IgM synthesis was inhibited instead of IgG. Further evidence has demonstrated that 4(R)-hydroxy-ochratoxin A, a metabolite of ochratoxin A, was as potently immunosuppressive as ochratoxin A in mice at dosages of 1 mg/kg b.w., resulting in 80–93% inhibition of spleen cells that synthesize IgM and IgG. However, another metabolite, ochratoxin A, did not work (Creppy *et al.*, 1983).

It has long been suspected that ochratoxin affects the humoral and cellular immune responses in chicken (Pier *et al.*, 1980). Leucocytopenia, especially lymphoey topenia, has been linked to ochratoxin. In broiler hens, heterophils' phagocytic, locomotory, and bactericidal activity was compromised (Chang *et al.*, 1979; Chang and Himilton, 1980). The reduced phagocytic activity was associated with themselves and not due to a serum factor, such as complement, Since ochratoxin A alone or in combination with aflatoxin B caused hypoproteinemia, lymphocytopenia, heterophilia, decreased complement activity, and regression of Bursa of Fabricius, Campbell *et al.* (1983) did not find any change in the phagocytic activity of heterophils or in the antibody titres to B. abortus and sheep RBCs in broiler chicks. Poultry studies have examined the direct effects of ochratoxin A on humoral and cellular immune responses (Dwivedi, 1984). Two to four parts per million of ochratoxin A caused a considerable decrease in serum immunoglobulin levels, specifically IgM, IgG, and IgA, in poultry (Dwivedi and Burns, 1984), and IgM and IgG levels in turkeys. Regression of the Bursa of Fabricius together with lymphoid depletion in the Bursa, spleen, caecal, Lonsils, and Peyers' patches seemed to be linked to the decrease of immunoglobulins in serum and immunocompetent tissues. In primary and secondary lymphoid tissues, ochratoxin A seriously damaged the progenitor cells (lymphocytes and plasma cells) (Dwivedi and Burns, 1984).

Ochratoxin A has been shown in electron microscopy experiments to induce necrosis and degeneration of lymphoid cells, including plasma cells, within the lymphoid organ (Dwivedi, 1984). This, along with observations of lymphoid depletion from the immunocompetent organs and reduction of bone marrow activity in chicks (Doupnik and Peckham, 1970; Packham *et al.*, 1971) and turkey poults (Chang *et al.*, 1981; Dwivedi and Burns 1984; 1985). Treatment with ochratoxin A indicates an immunosuppressive impact. Ochratoxin A has been shown to have a more significant impact on CMI response. Fowls and turkeys were found to have significantly lower delayed hypersensitivity (DH) reactions to avian tuberculin, phytohaemagglutinin, dinitrochlorobenzene, and bovine serum albumin in a dose-related manner. The splenomegaly response in chick embryos, which measures the graft-versus-host reaction (GVHR), was found to be much lower in broilers treated with ochratoxin A. Likewise, turkeys and fowls showed a decreased antibody response to bovine serum albumin (Dwivedi, 1984; Burns and Dwivedi, 1986). Quail treated with 4 and 8 ppm ochratoxin A also showed a decrease in delayed hypersensitivity symptoms. In an in vitro investigation, Klinkert *et al.* (1981) found that ochratoxin A caused a 56% suppression of macrophages, a T cell function, from guinea pigs. According to these

research, ochratoxicosis causes a dose-related depression in immunological responses, particularly CMI, with the effects being most pronounced in poultry, followed by turkeys and quail. The immune responses were not significantly lowered in quail and ducks because lymphoid organs were not significantly impacted (Burns and Dwivedi, 1984; 1986).

As evidenced by the higher incidence of air sacculitis in field outbreaks of ochratoxicosis in broiler fowls, the immunosuppressive action of ochratoxin A has practical implications due to the increased susceptibility of affected hosts to secondary infections (Hamilton *et al.,* 1982). It is important to keep in mind that ochratoxin may have negative impacts on the protection that vaccination programs are supposed to provide.

Humoral and cell mediated immunologic measurements were evaluated to determine the effects of ochratoxin A on immune function in swine. Cutaneous basophil hypersensitivity to phytohemagglutinin (PHA), delayed hypersensitivity to tuberculin, PHA-induced lymphocyte blastogenesis, interleukin - 2 productions, total and isotype Lmmunoglobulin concentrations, antibody response to chicken RBC, and Immune functions were assessed using macrophage activation. Gilts treated with ochratoxin A showed decreased interleukin-2 production when lymphocytes were stimulated with concanavalin A, decreased cutaneous basophil hypersensitivity response to PHA, decreased delayed hypersensitivity to tuberculin, decreased macrophage number and phagocytic activity, and decreased stimulation index for lymphoblastogenesis. Humoral hemagglutination (chicken RBC) titre and total and isotype immunoglobulin concentrations did not differ. These findings suggest that in developing pigs, ochratoxin may inhibit the cell-mediated immune response. Sharma (1993) reported that ochratoxin A had immunosuppressive effects.

Public Health Aspect of Ochratoxin A

Almost all animal species, including primates, have been shown to be toxically affected by ochratoxin A. As a result, the poison will undoubtedly also affect the human kidney. Ochratoxin A can enter the human food chain in two ways: (a) directly through plant products like cereals and finished goods, and (b) indirectly through ochratoxin A residues in animal-based foods ("carryover"). Significant levels of ochratoxin A have been detected in coffee beans, barley beer, and wheat flour and bread. The situation is made more difficult by the discovery of ochratoxin A residues in milk, eggs, and edible tissues of slaughtered animals (pigs and poultry), especially when there are no visible macroscopic lesions or indicators. It has been discovered that country cured ham and sausages contain ochratoxin A-producing fungal strains. It's interesting to note that ochratoxin A reached a depth of 0.5 cm in beef and 10 cm in cheese. Cooper and associates (1982). The function that ochratoxin A plays in producing abortion and embryotoxic, teratogenic, and carcinogenic consequences is of special public health concern. Ochratoxin A-induced immunosuppressive effects can have far-reaching ramifications since the afflicted host may experience latent secondary bacterial, viral, or parasite infections, and the immunization program may be negatively impacted. Ostratoxin A-induced nephropathy in pigs and endemic (Balken) nephropathy, a deadly kidney disease that affects people in parts of Yugoslavia, Bulgaria, and Romania, have been found to be strikingly comparable. Given that ochratoxin A has been found in the food consumed by impacted

households and in the blood of people from hyperendemic areas (Plestina *et al.,* 1980; Hult *et al.,* 1980; 1982), a strong causal association between ochratoxin A and endemic (Balkan) nephropathy has been proposed (Krogh, 1978). Furthermore, it has been discovered that the incidence and mortality rates of Balkan endemic nephropathy are closely linked to a high incidence of urinary tract tumors in Bulgaria and Yugoslavia (Ceovic *et al.,* 1976; Chernozemsky *et al.,* 1977). However, the overall amount of ochratoxin A that humans consume has not yet been determined and requires more research.

Mycotoxin and Its Economic Significance

According to estimates from the Food and Agriculture Organization (FAO), mycotoxins impact 25% of global food crops annually. At practically every stage of the marketing process between producer and consumer, mycotoxin-contaminated products pose serious economic and trade issues (Dawson, 1991). Both industrialized and developing nations are beginning to recognize the importance of mycotoxins in international trade. The export of agricultural products such peanuts, cotton seeds, copra, and their derivatives has been impacted in recent years (Huff *et al.,* 1983). The highest-quality batches of these commodities are exported from emerging nations, while inferior goods that are unsuitable for international consumers are distributed and sold domestically. There are two types of economic losses: direct and indirect. Reduced agricultural yields for growers, decreased animal performance, and higher losses from livestock diseases are all examples of direct losses. Mycotoxin's indirect economic repercussions include likely causing a complete loss of food or feed, lowering the crop's sell price, and making it unsellable. Additionally, there are significant increases in the expense of insect or fungicide treatment. Due to litigation and the need for compensation, the traders who act as middlemen in the agricultural produce trading chain suffer losses. According to FAO (1977), consumers bear the financial burden of reduced health and productivity, as well as potential medical and veterinary expenses. Many nations have specific laws on mycotoxins in foods and feed (Schuller *et al.,*1983; Labuza,1983). Aflatoxin tolerance is the main focus of the restrictions, which are typically in the parts per million ng/g range for aflatoxin Bl and the subrange for aflatoxin M1. For instance, the tolerance for total aflatoxins in nuts and nut-based products in Canada is 15 parts per billion. Denmark, Belgium, and the Soviet Republic regulate ochratoxin A; Norway, Sweden, Switzerland, and Belgium regulate patulin; Belgium regulates sterigmatocystin and zearalenone; the USSR regulates trichothecenes in general; and Canada regulates deoxynivalenol (Schuller *et al.,* 1983; Van Egmond, 1989).

Control of Mycotoxins

The detrimental effects that undesired mycotoxin levels in food and feed sources may have are becoming more widely recognized. Food contamination and nutrition are negatively impacted by the presence of infected food. The inherent risks of tainted food or feed have sparked an extraordinary research effort to create a cost-effective and efficient control mechanism. However, extensive observation has shown that the effectiveness of the control technique may be limited (Lillehoj and Wall, 1987). Mycotoxin control is based on three basic principles: prevention, removal, and detoxification. The first approach is seen to be superior to the other two because the latter two could degrade the quality of the products.

If proper storage conditions are followed, the generation of toxins can be avoided. Grain that is being stored should be kept mold-free and inspected on a regular basis. This involves checking the temperature, moisture content, and thoroughly examining it for insect infestation, microbial infection, foreign objects, and broken seeds. Modifying the environment, regulating temperature and moisture either separately or in combination, or even using chemical preservatives can all help prevent the establishment and development of mold in storage. (Scott, 1989).

Maintenance of the altered atmosphere when the novel technology of hermetic grain storage was proposed. Because of this, the systems are frequently unavailable in tropical nations; fumigation is frequently employed as a substitute method of controlling insects. Phosphene fumigation is a common practice in tropical nations since it is inexpensive, simple to use, and efficient at controlling pests and insects in grain (Bond, 1984).

Based on the chemical destruction of the toxin in situ, the process currently seems to provide economical and efficient detoxification. According to Fouler *et al.* (1994), ochratoxin can be detoxified by heating it with hydrogen peroxide in an alkaline environment. The most effective and useful inactivation approach is ammonia in gaseous and aqueous solution.

Therefore, in addition to informing farmers and consumers about the dangerous effects of mycotoxins, conducting routine surveys and analyses of grains can help reduce the issue of mycotoxin entrance into the human food chain. The government and academia are working together to discover the realistic mycotoxin management technologies that will support an integrated strategy to mycotoxin control, which will ultimately result in a safe food supply.

References

Amita, P., 2001. M.V.Sc. thesis, Univ. Agric. Sci., Bangalore.

Bach, P. H., Gregg, N. J. and Delacruz, L, 1992. Food Chem. Toxicol., 30 (3) 205-211.

Bendele, A. M., Carlton, W. W., Krogh, P. & Lillehoj, E. B., 1985. J. Natl Cancer Inst., 75 (4): 733–742

Bhanuprakash., 2002. M.V.Sc. thesis, Univ. Agric. Sci., Bangalore.

Bodnarchuk, A. I. and Karpruk, I. M, 1984. veterinariya, Moscow, Abstracted in Poultry 10 : 135.

Bond, E. J, 1984. In: A Manual of Fumigation for Insect Control. FAO Plant Production and Protection paper No. 54, Rome, FAO pp 432.

Boorman, G. A., Hong, H. L., Dieter, M. P., Hayes, H. T., Pohland, A.E., Stock, M. and Luster, M.I: 1984. Toxicol. & Appl. Pharmacol, 72:304

Breitholt, Z., Emanuelsson, A., Olsen, M., Oskarsson, A., Palminger, 1. and Hult, K.,1993. J. AOAC. Int, 76: 842-846

Brown, M. H., Szczech, G. M. and Purmalis, B. P., 1976. Toxicol. Appl. Pharmacol. 37 (2): 331-338.

Buckle, A. E. 1983. Vet. Res. Commun. 2: 171-186.

Burns, R. B and Dwivedi, P., 1984. In Mycotoxins in Animal and Human Health, Edinburgh, Scotland.

Burns, R. B. and Dwivedi, P., 1986. Poult. Sci. J. 42 (1) : 48 - 55.

Campbell, M. L., (Jr), May, J. D., Huf/, W. E., and Doerr, J. A'J 1983. Poult. Sci. 62: 2138 - 2144.

Castegnaro, M. and Cheronohemsky, I. N. 1987. Cancer Res. 47 : 3608

Ceovic, S., Grims, P. and Mitar, J., 1976. Lijee vjesn 98: 301-304.

Chang, F. C. and Chu, F. S., 1977. Food Cosmet. Toxicol. 15: 199 - 204

Chang, C. F., Huf/, W. E., and Hamilton, P.B:1 1979. Poult. Sci. 58, 555 - 558.

Chang, C. F., and Hamilton, P.B.,1980. J. Environ. Microbiol. 39 : 572-575

Chernozemsky, l. N., Stoyanov, l. S., Petkova Bocharova, T. K., Nicolov, I. G., Draganov, I. V., Stoichev, 1 .1., Tanchev, Y., Naidenov, D, and Kalcheva, W. D'l 1977. Int. J. Cancer, 19: 1-11.

Christensen, C.M. and Kaufmann, H.H., 1969. Grain storage: The role of Fungi in Quality 1055. University of Minnesota Press, Minneopolis, pp. 92. Cited by: Dwivedi and Burns, 1985, Res. Vet. Sci., 36: 117-121

Chandrasekaran, D., 1996. Proc. 20th World Poult. Cong., New Delhi, 4: 268.

Chu, F. S., 1971. Arch. Biochem. Biophvs. 147: 359-366

Chu, F. S., 1974. Biochem. Pharmacol. 23: 1105 - 1113.

Chu, F. S and Butz, M. E, 1970. J. Assoc. Offic. Anal. Chem. 53: 1253-1257.

Cooper, S., Wood, G., Chapman, W. and Wiliiams, A., 1982. Proc. vet. lnt. Symp. mycotoxins and phycotoxins, Vienna, Austria. pp. 64-67

Creppy, E. E., Lorkowski, G., Roschenthaler, R. and Dirheimer, G.,1982. Proc V Int. Symp. Mycotoxin and Ph yeo-toxins Vienna, Austria. pp 289-292.

Creppy, E. E., Stormer, F. C., Roschenthaler, R, and Dirheimer, G., 1983. Infection and Immunity 39: 1015-1018

Devegowda, G., Raju, M.V.L.N., AFZAL, N. and Swamy, H.V.L.N., 1998. In: Biotechnology in the feed Industry. Eds. T.P. Lyons and K.A Jacques, Proc. 14th Alltechs Annual Symp., KY, USA pp. 241-255

Devi, G.R. and Polasa, H., 1982. Curr. Sci., 51: 751

Dawson, RJ. 1991. In: Fungi and Mycotoxins in stored products. AC!R proceeding No.B6 Cham, PBR, Highley Hocking, AD and Pitt J.I., (eds) The Griffin Ltd. Netly, South Australia. pp. 22-28.

Di Paolo, N., Guarneri, A., Loi, F., Sacchi, G., Mangiarotti AN. and Di Paolo,M:. 1993. Nephron. 64 (4) : 621-625.

Doupnik, B,. (Jr) and Peckham, J. C.,1970. Appl. Microbiol. 19: 594-597.

Dwivedi, P., 1984. PhD Thesis, University of Edinburgh, Scotland.

Dwivedi, P., 1988. In : Advances in Toxicology and Environmental health edited by Gupta P.K and Ravi Prakash. V Jamnagar Book Agency, New Delhi, pp 203-251.

Dwivedi, P. and Burns, R. B. 1984. Res. Vet. Sci. 36: 92-103

Dwivedi, P. and Burns RB., 1984c. Res. Vet. Sci. 36: 117-121.

Dwivedi, P. and Burns, R. B.,1985. Avian Path., 14: 213-225.

Egmond, H.P.V. and Spijers, G.J.A., 1994. J. Natural Toxins, 3: 125-144.

F. A. 0 1977. Mycotoxins. Report of the Joint FAO /wHO/ UNEP Conference on mycotoxins, Nairobi 19-27 September 1977. Rome, Food and Agriculture, Organization of the United Nations. pp.1 05 (FAO food and Nutrition paper 2)

Fouler, S. G., Trivei, A. B. and Kitabatake, N., 1994. AOAC, 77(3): 631-637.

Fukui, U., Hayasaka, S., ltoh, M. and Takeuchi, Y. 1992. Neurotoxicol. Teratol. 14 (3): 191-196

Galtier, P., 1974. Ann. Rech. Vet., 5, 311-318

Galtier, P., Camguilhem, R and Bodin, G., 1980. Food. Cosmet. Toxicol. 18 (5) 493-496.

Gaur, Harlans, K., Singh, B. and Raina, J.S., 1991. Indian J. Poult. Sci., 52: 2206-2211.

Hald, B., Wood, G.M., Boenke, A., Schurer, B. and Finglas, P., 1993 Food Addit. Contam. 10 (2): 185-207.

Hamilton, P. B., Huff, W. E., Harris, J. R. and Wyatt, R. D., 1982. Poult. Sci. 61: 1823 - 1841.

Hayes, A. W., Hood, R. D. and Lee, H. L. 1974. Teratology. 9: 93-97.

Hood, R. D., Naughton, M. J. and Hayes, A. W., 1976. Teratologv 13: 11-14

Huff, W. E., Wyatt, R. D., Tucker, T. L. and Hamilton, P. B .1974. Poult. Sci. 53: 1585-1591.

Huff, W.E, Wyatt R.D and Hamilton, P.B. 1975. J. Microbial, 30: 48-51.

Huff, W.E. and Doerr, J.A, 1981. Poult. Sci. 60: 550-555.

Huff, W. E., Doerr, J. A., Wabeck, C. J., Chaloupka, C. W., MaY, J. and Merkeley, J. W. 1983. Poultrv Sci., 62 (9): 1764-1771.

Hult, K., Teiling, A. and Gatenbeck, Sy 1976. Appl. Environ. Microbial. 32(3): 443 - 444.

Hult, K., HokbY, E., Gatenbeck, S., Plestina, R. and Ceovic, S, 1980. Proc. lnt. Union Pure Appl. Chem. Round., 4th 35, Abst.717.

Hult, K., Plestina, R., Ceovic, S., Habazin-Novak., V. and Radic, B. 1982. Proc. V. lnt. Svmp. Mvcotoxins and Phvcotoxins vienna. pp 338 - 341

Hutchinson, R. D., Steyn, P.S. and Thompson, D.L. 1981. Tetrahedron. Letters 43: 4033-4036.

Kanisawa, M.,1984. In: Kurata, H. & Ueno, Y., eds., Toxigenic Fungi-Their Toxins and Health Hazard, Tokyo: Kodansha and Amsterdam: Elsevier, pp. 245–254.

Kanisawa, M. & Suzuki, S. 1978. Gann., 69, 599–600.

Klinkert, W., Lorkowski, G., Creppy, E. E., Dirheimer, G. and Roschenthaler, R. 1981. Toxicol. Eur. Res. 3: 187-189.

Krogh, P. 1976. In: Advances in Veterinary Science and comparative Medicine, Academic Press New York. Vol. 20, pp.147-170.

Krogh, P. 1977. Nord. Vet. Med. 29: 402-405.

Krogh, P. 1978. Acta. Patholo. Microbial. Scand. Sect. A Suppl No. 269. pp.1-28.

Krogh, P., 1987. In: Mycotoxins in Food. Ed. P. Krogh, Academic Press, London, pp. 94-121.

Krogh, P., Elling, F., Hald, B., Jylling, B., Petersen, V. E., Skadhauge., E and Svendsen, C.K. 1976a. Acta Patholo. Microbiol. Scand. Sect. A 84 : 215-221.

Krogh, P., Elling, F., Hald, B., Larsen, A. E., Liliehoj, E. B., Madsen, A. and Mortensen, H. P. 1976b. Toxicology, 6: 235-242.

Krogh, P., Elling, F., Gyrd-Hansen, H., Hald, B., larsen, A. E., Liliehoj, E. B., Madsen, A., Mortensen, H. P and Ravnskov, U. 1976c. Acta. Pathol. Microbiol. Scand. Sect A. 84: 429-434.

Kumari. D., and Sinha, S. P. 1994. Food Chern. Toxicol. 32 (5): 471-475.

Labuza, T. P. 1983. J. Food Protect. 46: 260–265

Lillehoj, E. B. and Wall, J. H. 1987. In Aflatoxin in maize Zuber, M. S., Liliehoj, E. B. and Renfro, B. L (eds). A proceedings of the Workshop. CIMMYT, Mexico, D.F. pp.260-279.

Madhyastha, M. S., Marquard, R. R. and Frohlich, A. A. 1992. Arch. Environ. Contam. Toxicol, 23 (4): 468-472.

Manickam, A., Palaniswami, A. and Neelakantan, S. 1985. Indian Vet. J. 62 (8) 711-744.

Marquardt, R. R. and Frohlich, A. A. 1992. J. Anim. Sci. 70 (12): 3941-3949

Mayura, K., Parker, R., Berndt, w. O, and Phillips, T. O. 1985. J. Environ. Microbiol. 48(6): 1186-

More, J. & Galtier, P. 1975. Ann. Rech. Vét., 6, 379–389.

Osborne, B.G. 1980. Food. Cosmet. Toxicol, 18: 615-617.

Patterson, D.S.P, Shreeve, B. J., Roberts, B.A., Berrett, S., Brush, P.J., Glancy, E. M. and Krogh, P. 1981. Res. Vet. Sci. 31: 213 - 218.

Peckham, J. C., Doupnik, B. Jr. and Jones, O.H. Jr. 1971. Microbiol. 21: 492-494.

Petkova-Bocharova, T. and Castegnar, O.M. 1985. Food Add. Contam. 2, 267-270.

Pfohl Leszkowiez, A., Grosse, Y., Kane, A., CreppY, E. E., and Dirheimer, G. 1993. Mutat. Res. 289(2): 265-273.

Pier, A. C, Richard, J. L. and Cysewski, S. J. 1980. J. Am. Vet. Med. Assoc. 176: 719 - 724

Plestina, R., Radic. B., Habzin-Novak, V., Ceovic, S., and Kratj, Z. 1980. Proc. Int. Union Mf2j. Chem. Round. 4th 35: Abst. 315.

Prior, M. G. and Sisodia, C. S. 1982. Canad. J. Comp. Med, 46: 91-96

Raina, J.S. And Singh, B., 1991. Indian J. Anim. Sci., 61: 671-676.

Reddy, B. N., Nusraih, M., Kumari, C. K. and Nahdi, S. 1983. Indian Phytopathol. 36 (4): 683 - 686.

Roth, A., Eriani, G., Dirheimer, G. and Gangloff, J. 1993. FEBS-Lett. 326 (1-3): 87-91.

Scott De, B., 1965. Mycopathol. Mycol. Appl., 14: 213-222.

Scott, P.M., Van Walbeck, W., Harwing, J. And Fennel, O.I., 1970. Can J. Plant. Sci. 50: 583-585. Cited in world's Poult. Sci. J., 32-47.

Scott, P.M., Van Welbeck, W., Kennedy, W. And Anyeti, W., 1972.J. Agri. Food Chem., 20: 1103-1108. Cited in: World's Poult. Sci. J., 42: 32-47

Schuller, P. L., Van Egmond, H.P. and Stoloff, L. 1983. Proceedings of the International symposium on mvcotoxins. Naguib, M. M., Park, D.L. and Pohland, A.E. (eds). Publishing Science Department (NIDOC) Dokki, Cairo, Egypt. pp.111-129.

Scott, P. M. 1989. Control of mycotoxins- an overview. In : Mvcotoxins and phvcotoxins. Natori,S., Hashimoto, K. and Ueno, Y. (eds) Elsevier Science Publishers, B. V. Amsterdam. The Netherlands pp. 127-134.

Sharma, R.P. 1993. Immunotoxicity of mycotoxins, J. Dairy Sci. 76 (3): 892-897.

Shirai, S., Ohshika, S. and Majima, A. 1985. Acta. Soc. Ophthal. Jap. 89 (6): 753-760.

Shotwell, D.L., Hesseltine, C.W. and Goulden, M.L., 1969. Note on the natural occurrence of

Steyn, P. S., Vleggaar, R., Du Preez, N. P., Blyth, A. A and Seegers J.C, 1975. Toxicol. Appl. Pharmacol. 3291: 198 - 203.

Thirumala Devi, K., Mayo, M.A., Reddy, G. and Reddy, D.V., 2002. J. Food Prot., 65 : 1338-1340.

Thyagarajan, D., Sundararasu, V. and Narahari, D., 1996. Proc. 20th World Poult. Cong., New Delhi, 4: 433-439

Szczech, G. M., Carlton, W. W., Tuite, J. and Caldwell, R. 1973a. swine Vet. Pathal. 10: 347-364

Szczech, G. M, Carlton, W. W., and TUite, J. 1973b. Vet. Pathol. 10: 2,19 - 231. '

Szczech, G. M., Carlton W. W., and Tuite,J. 1973c. Vet. Pathal. 10: 135 -154.

Szczech, G. M. and Hood, R. D. 1981. Taxicol & Rl. Pharmacol. 57: 127-137.

Valenta, H., Kubn, l. and Rohr, K. 1993.Chromatogr., 613 (2) 295-302.

Van Der Merwe K. J., Steyn, P.S., Fourie, L., Scott, DE. B. and Theron, J.J., 1965. Nature (London), 205: 1112-1113

Van Egmond, H. P. 1989. Food. Addit. and Contam., 6: 134-188.

Verma, R. J., Kolhe, A. S. and H. C. Dube, 1994. Indian Phytopath, 49 (1) : 62-66.

Visconti, A. and Bottalico, A. 1983. Aqric. Food. Chem. 31: 1122 - 1123

Zohri, A. A., and Saber, S. M, 1993. Zentralbl - Mikrobiol. 148 (5): 325-332.