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Review Article

Ochratoxicosis: A Possible Threat to Public Health and Animal World

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Abstract

Mycotoxicosis is one of the major havoc to the poultry and pig industry. The modern studies revealed severe toxic potential of mycotoxins including carcinogenic, teratogenic and genotoxicity potential. Among several mycotoxins, Ochratoxin is one of the major public health concern toxicant. Ochratoxins are produced from *Aspergillus ochraceus* and *Penicillium verrucosum.* Amongst eight Ochratoxins, Ochratoxin A (OTA) is considered to be most pathogenic. OTA produced nephrotoxicity by oxidative damage and inhibition of protein synthesis. Mitigation of toxicity can be done by following rules and regulations and also by detoxification aiming at biological and chemical methods. Thus it is important to discuss the pathogenic role of the mycotoxins, its mechanism of toxicity, susceptible host, target organ and other epidemiological findings.

Keywords: Ochratoxins; Mitigation; Nephrotoxicity; Carcinogenicity.

Introduction

The modern day farm and managemental practices aim at more profitability at short duration of time. Thus a tiny mistake at that level may incur heavy financial loss. A common perception about is that anthropogenic toxicants are more toxic than the natural ones for example mycotoxins includes aflatoxin, ochratoxins, trichothecens, zearlenone, citrinin , ergot alkaloids etc. Mycotic growth leads to generation of several secondary metabolites i.e. fungal or mycotoxins. These mycotoxins have different target organ for toxicity. Ochratoxins are one of the major mycotoxins that reduce the productivity of the animals amongst mycotoxins. According to Tapani et al., (2000) [1], around 500 mycotoxins have been documented. There are approximately, 300 mycotoxins are potentially toxic to animals and humans [2]. Ochratoxins are not only in focus due to clinical and sub clinical intoxications in livestock but also nephric impairments in human [3]. Ochratoxin A (OTA) is one of the several fungal mycotoxins that have raised significant public health concern throughout the world. OTA exposure is known as Ochratoxicosis, and kidney tissue is the major primary affected target organ. International agency for research on cancer (IARC) has classified OTA as a possible carcinogen (Group 2B) to humans.

Sources of Ochratoxins

Ochratoxin A (OTA) is a secondary toxic metabolite produced mainly by some strains of *Aspergillus ochraceus* and *Penicillium verrucosum species. Aspergillus* are habitat of tropical regions, whereas *Penicillia* are of temperate regions; and can grow when the temperature is as low as 5 degree

Celsius [4]. *Aspergillus ochraceus (A. ochraceous),* was the first fungi from which it was isolated and named Ochratoxins. Among all species of Aspergillus, *A. carbonarius* produces the highest quantities of this mycotoxin [5]. According to EFSA (2004) [6], highest reported occurrence of OTA was found in cereal grains and to a lower extent in other foodstuff of plant origin (i.e., wine, coffee, beer, spices and chocolate).

Ochratoxins are a Group of Eight Compounds:

1. Ochratoxin A (OTA)
2. Ochratoxin B (OTB)
3. Ochratoxin C (OTC)
4. Ochratoxin A ethyl ester,
5. Ochratoxin A methyl ester,
6. Ochratoxin B ethyl ester,
7. Ochratoxin B methyl ester and
8. 4-Hydroxyochratoxin A.

- Ochratoxin A (OTA), OTB and OTC are the toxic members of the group, with OTA being the most toxic one. It is white, odorless and crystalline solids with a molecular formula of $C_{20}H_{18}Cl$. The basic chemical structure is derived from isocoumarin and L-β-phenylalanine, and is biosynthetically classified as pentakeptide.

Mechanism of Toxicity

Ochratoxins produce mainly nephrotoxicity. It mainly affects protein synthesis and subsequently DNA and RNA synthesis. It acts as competitive inhibitor on phenylalanine-t RNA ligase, thus reduces protein synthesis. At proximal convoluted tubule, ochratoxins inhibit the enzyme phosphoenolpyruvate carboxylase, thus alters the structural and functional capacity of nephric system to metabolize calcium. This will lead to degeneration and necrosis of renal tubule and also atrophy and sclerosis of the proximal tubules. Furthermore, it also hampers oxidative pathways and aggravates nephric impairment. Carcinogenicity and genotoxicity has also been mentioned by Ochratoxicosis.

Nephrotoxic Potential of Ochratoxin A

- Porcine nephropathy, associated with OTA exposure was first time identified in Denmark. The toxicity is characterized by enlargement and discoloration of nephrons and a subsequent accumulation of uric acid. Histopathological examination characterizes nephropathy by degenerative and atrophic changes in proximal and distal convoluted tubules alongside with interstitial fibrosis. Microscopically glomerulo-nephrosis, tubulonephrosis, focal tubular epithelial cell proliferation and multiple adenoma-like structures in the renal parenchyma also revealed potent nephrotoxic potential of Ochratoxin A [7].
- Epidemiological studies done by Hamilton et al. (1982) [8] showed five independent cases of Ochratoxicosis in about 970,000 turkeys, two in about 70,000 laying hens and in about 12,000,000 broiler chickens respectively. Dwivedi and Burns (1986) [9] advocated that kidney as the target organ of OTA for poultry as it seemed to be in rest of the species.
- Ochratoxin A is more potent and less acute than Citrinin. OTA acts on both proximal and distal tubules thus resulting in a severe loss of both fluids and electrolytes due to less site specificity. Pigs are generally considered as the animal species most sensitive to the nephrotoxicity of OTA [10].
- Poultry industry is also affected by OTA contamination. Turkeys, chickens and ducklings are susceptible to this toxin. Typical signs of poultry Ochratoxicosis are reduction in weight gain, poor feed conversion, reduced egg production, poor egg shell quality and nephrotoxicity.
- Several studies have been done regarding toxicopathological role of Ochratoxins in poultry. Verma et al., (2004) [11] showed reduction in egg production and egg weight in laying hens when fed a diet contaminated with OTA at 2 and 3 mg/kg levels. OTA exposure @ 2.5 mg OTA/kg also reduced the concentration of α- tocopherol in the chicken liver [12]. Even at 0.25 mg/kg of OTA level chicken immune system shows immunosuppressant action [13].

Immune System and Ochratoxins

Ochratoxin A is an immunosuppressant fungal compound. The immunosuppressive activity of OTA is characterized several clinical evidences as-

- Reduction in size of vital immune organs,
- Reduced antibody titre
- Alterations in the numbers and functions of antibody responses
- Alterations in number and function of cells of immune system,
- Modulation in production of cytokines [14]

- Chang et al. (1981) [15] stated Ochratoxin produced bone marrow activity suppression, depletion of lymphoid tissue and thymus regression in turkey poults. Dwivedi and Burns, (1984b) [16] also reported reduction in levels of IgG, IgA and IgM in lymphoid tissues and serum of chicken following OTA contaminated feed administration at dose level of 2-4 ppm for 20 days.

Regulations regarding Ochratoxins

- By the end of 2003, on a worldwide basis, at least 99 countries had mycotoxins regulations for food and/or feed. Guidance values have been sanctioned for a further five mycotoxins including Ochratoxin A under Commission Recommendation 2006/576/EC.

Feed Commodities	Maximum Level (µg/kg)
Cereals and cereal products	250
Completary and complete feedstuffs for pigs	50
Completary and complete feedstuffs for poultry	100

- The Commission of the European Communities Recommendation (2006/576) guidance values for OTA in feedstuffs.

Methods to Mitigate/ Control Effects of Ota in the Animal Industry

OTA toxicity can be mitigated by several detoxification methods. Detoxification can be done by following methods as:

A. *Chemical Methods*-by using adsorbents as Activated charcoal, Hydrated Sodium Calcium Aluminosilicate (HSCAS), Bentonite etc.

B. *Biological Methods*

- By using herbal extracts- with extract of artichoke.
- By using yeast- using *Saccharomyces cerevisiae* strain 1026 and probiotic yeast culture *Saccharomyces boulardii* (10 mg/kg of feed).
- By using rumen microflora- *Clostridium sporogenes* and *Lactobacillus vitulinus* [17]
- By using prebiotic as Mannose oligosaccharide (MOS) etc.

Conclusion

Ochratoxin A is highlighted mainly due to possible carcinogenicity and nephrotoxicity declared by the International Agency of Research on cancer (IARC). Many toxicopathological studies revealed symptoms as of nephrotoxicity, immunosuppression etc. Due to public health concern and severe loss to animal and poultry industry, it is mandatory to control mycotoxicosis for future health and economics.

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