

Journal of the Hellenic Veterinary Medical Society

Vol 72, No 4 (2021)



Ochratoxin A occurrence, its pathological effects on poultry health and decontamination approaches

U MEHTAB, MA TAHIR, RZ ABBAS, A ABBAS, K HUSSAIN, F SIDDIQUI, M MOHSIN, Z RANI, A REHMAN, R YASIN

doi: [10.12681/jhvms.29355](https://doi.org/10.12681/jhvms.29355)

Copyright © 2022, U MEHTAB, MA TAHIR, RZ ABBAS, A ABBAS, K HUSSAIN, F SIDDIQUI, M MOHSIN, Z RANI, A REHMAN, R YASIN



This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0](https://creativecommons.org/licenses/by-nc/4.0/).

To cite this article:

MEHTAB, U., TAHIR, M., ABBAS, R., ABBAS, A., HUSSAIN, K., SIDDIQUI, F., MOHSIN, M., RANI, Z., REHMAN, A., & YASIN, R. (2022). Ochratoxin A occurrence, its pathological effects on poultry health and decontamination approaches. *Journal of the Hellenic Veterinary Medical Society*, 72(4), 3257–3262. <https://doi.org/10.12681/jhvms.29355>

Ochratoxin A occurrence, its pathological effects on poultry health and decontamination approaches

U. Mehtab¹, M.A. Tahir¹, R.Z. Abbas², A. Abbas^{*1}, K. Hussain¹, F. Siddiqui³,
M. Mohsin⁴, Z. Rani², A. Rehman¹, R. Yasin¹

¹Department of Veterinary and Animal Sciences, Muhammad Nawaz Shareef University of Agriculture Multan, Pakistan

²Department of Parasitology, University of Agriculture Faisalabad, Pakistan

³Department of Microbiology, Cholistan University of Veterinary & Animal Sciences, Bahawalpur, Pakistan

⁴College of Life Sciences, Fujian Agriculture and Forestry University, China

ABSTRACT: Mycotoxins are filamentous fungi which can be seen microscopically and they impart adverse effects on poultry health. The occurrence of mycotoxins in poultry feed imparts adverse effects not only to the birds' health but also causes huge economic losses by affecting feed conversion ratio, production of meat and eggs, and also responsible for histopathological changes in lymphoid organs of chicken. More than 300 different species of mycotoxins have been reported from which the ochratoxin and aflatoxins are the most harmful for poultry industry. Among ochratoxins, especially the Ochratoxin A (OTA) is produced from *Aspergillus Ochraceus* and *Penicillium verrucosum* species as storage fungi inside stored grains and feed ingredients. The ochratoxicity is a dose-dependent factor and hits the immune system of birds besides decreased feed intake and decreased body weight. Higher doses of OTA toxicity resulted in deterioration of egg shell quality and hatchability in layers and breeders. Histopathological profile of ochratoxicity affected birds showed severe to moderate changes in the kidney, bursa of Fabricius, liver, thymus, spleen, heart, and lungs depending on dosage. In this review article, an attempt has been made to concise the OTA associated alterations in growth pattern, production index, biochemical changes and histopathological profile of the poultry. The current approaches and agents (Vitamin-E, Silymarin), which are being used to reduce the effects of OTA toxicity in birds, have also been discussed.

Keywords: Ochratoxins, Poultry, Immunity, Biochemical changes

Corresponding Author:

Dr Asghar Abbas, Department of Veterinary and Animal Sciences, Muhammad Nawaz Shareef University of Agriculture, Multan, Pakistan
E-mail address: asghar.abbas@mnsuam.edu.pk

Date of initial submission: 16-11-2020
Date of acceptance: 27-01-2021

INTRODUCTION

The poultry sector is an important and vibrant segment of agriculture which plays important role in national economy of many countries (Zhang *et al.*, 2020; Khater *et al.*, 2020; Yasim *et al.*, 2020). However, its progress is affected by various diseases including mycotoxins (Baran *et al.*, 2020; Elmossalamy *et al.*, 2020; Shoaib *et al.*, 2020; Sugiharto *et al.*, 2020). Mycotoxins occurrence is global issue with strong economically negative impact on health of livestock, poultry and humans (Ali *et al.*, 2020; Moussa *et al.*, 2020; Lin *et al.*, 2020). Among mycotoxins, ochratoxin is a well-known toxin that survives in the agriculture and livestock sector damaging the cereal grains, poultry and livestock by-products (Ghonaimet *et al.*, 2020; Imran *et al.*, 2020; Khaskheli *et al.*, 2020). Several fungi species like *Aspergillus ochraceus*, *Aspergillus carbonarius*, *Aspergillus niger* and *Penicillium verrucosum* are responsible for ochratoxin production due to un-hygienic and improper storage of products under optimal temperature and humid conditions (Kembo *et al.*, 2020). Ochratoxin (OTA) is a chemically stable compound and its toxicity cannot be averted by adopting normal food storage procedures. OTA is found as a deleterious and carcinogenic substance in contrast to other live species. In animals, the kidneys is the chief target organ for OTA (Joint *et al.*, 2002; Duarte *et al.*, 2011; Kembo *et al.*, 2020). Immunosuppression and immune toxic effects are also reported due to OTA (Bondy and Pestka, 2000). Other deleterious effects of OTA includes the increased lipid peroxidation, mitochondrial damage and reduced macromolecules formation (Tinelli *et al.*, 2019).

During the last decade, several scientific studies have been conducted on mycotoxins to check their presence in the agriculture fields (Jarvis and Miller, 2005). Wang *et al.* (2006) confirmed different studies regarding the airborne presence of *Aspergillus* and *Fusarium* species in poultry sheds ranging from 361.3 and 74.6 CFU/m³ and taken as toxicogenic.

Toxico-pathological mechanism of *Alternaria* toxins (plants such as oilseeds and cereals) includes genotoxicity, cytotoxicity, teratogenicity and fetotoxicity which were hazardous to animal health (Kembo *et al.*, 2020). Mycotoxin contaminated poultry houses were reported by researchers due to unhygienic environmental conditions taking both the birds and workers at risk by inhaling the toxic air. The adverse effects of mycotoxins have made scientists to ponder in order to abate the escalating OTA in food chain

supplies to overcome the economic crises globally (Wang *et al.*, 2006). Similarly, in poultry sector the major devastating mycotoxins includes the aflatoxins (AF), ochratoxin A (OTA), fumonisins (FUM), deoxynivalenol (DON) and T2 toxin (Ghor *et al.*, 2020). Mycotoxin type-2 is considered 10 to 20 times more toxic when absorbed by the digestive system instead of inhaled, similarly 20 to 40 times more toxic if absorbed through the skin (Schleibinger *et al.*, 2004). Regarding the economic losses caused by OTA in the poultry include the stunted growth, poor FCR and enhanced mortality ratio. Peanuts and cereal grains are most commonly affected by mycotoxins globally and their 100% removal is still not possible. (Vieira *et al.*, 2004; El Miniawy *et al.*, 2014; Khatoon *et al.*, 2016). The different studies through toxicity testing approved the oral median lethal dose (LD 50) of OTA as 2-4mg/kg in chicken, 5.9 in turkeys and in quails& ducks 16.5 (Elaroussi *et al.*, 2006, 2008; Santin *et al.*, 2002).

Initially the OTA was discovered at Balkan region, but currently it is present around the globe due to its favorable growth rate in storage components under optimum conditions (Bui-Klimke *et al.*, 2014; Khatoon *et al.*, 2017; Sharif *et al.*, 2018). The OTA elimination is still a major issue in poultry sector due to its capability to survive the higher temperature. However, several different approaches are now approved for reduced OTA contamination at all levels. This review article summarizes the OTA associated alterations in growth pattern, production index, biochemical changes and histopathological profile of poultry. The current approaches and agents (Vitamin-E, Silymarin), which are being used to reduce the effects of OTA toxicity in birds, have also been discussed in the following sections.

Table 1 shows International standards and codes of practice to limit exposure to mycotoxins from certain foods established by the Codex Alimentarius Commission based on JECFA assessments.

These tolerable daily intakes are used by governments and international risk managers, such as the Codex Alimentarius Commission, to establish maximum levels for mycotoxins in food. The maximum levels for mycotoxins in food are very low due to their severe toxicity. For example, the maximum levels for aflatoxins set by the Codex in various nuts, grains, dried figs and milk are in the range of 0.5 to 15 µg/kg (a µg is one billionth of a kilogram). The Codex maximum limit for patulin in apple juice is 50 µg/L.

Table 1: Approved Level of OTA Species in Poultry Feed (JECFA, 2001)

OTA- Spp.	Optimal Temp.Range (Min-Max) °C	Water Activity	Affected Food Products
<i>Ochraceus</i>	24-31 (8-37)	0.95-0.99	chickpeas, rapeseed, pepper, and sesame seeds, nuts, oats rice, grain, maize, wheat, flour, and grain, espresso beans.
<i>Ochraceus carbonarius</i>	32-25	0.82	Grapes and grape items, including table grapes, wines, and dried vine organic products.
<i>Ochraceus niger</i>	35-37 (6-47)	0.77	Nuts, apples, pears, peaches, citrus, grapes, figs, strawberries, mangoes, tomatoes, melons, onions, garlic, and yams.
<i>Ochraceus verrucosum</i>	20 (0-30)	0.80	Oat crops; cheddar, meat items.

Chemistry of Ochratoxins

Ochratoxins are toxic metabolites consisting of dihydro-isocoumarin moiety linked with a phenylalanine through an amide bond. The chemical and physical properties involve the molecular weight of 403.8, being a white, odorless and heat stable crystalline substance having a melting point of 168-173°C resisting the 3 hours of sterilization process at 121°C (Koszegi *et al.*, 2013). Its partial degradation is noted at 250°C (Trivedi *et al.*, 1992). The OTA exhibits a strong fluorescence due to its specific structure property and existed in non-ionic, monoanionic and dianionic forms depending upon the microenvironment (Poór *et al.*, 2013; Kembo *et al.*, 2020).

Pathophysiology of Ochratoxins

Ochratoxins (OTA) is the causing agent of nephropathy and increases the incidence of renal carcinomas and adenomas in rats. Pathophysiological studies revealed that OTA acts on different sites along the nephron. Acute OTA exposure leads to an impairment of postproximal nephron function, predominantly of the collecting duct, resulting in altered electrolyte and titratable acid excretion (Pozo *et al.*, 2013). After activity of poison it assimilates into alimentary canal, wherever it ties with egg whites which supplies OTA an extended half-life from few days to month, depending on plasma grouping (Roth *et al.*, 1988; Berger *et al.*, 2003; Lino *et al.*, 2008). In rabbits, OTA is extremely cytotoxic and may cause hemolysis in red blood cells (Jan *et al.*, 2017). Low doses of OTA cause influence energy metabolism (amino acid, co-factors, vitamins and carbohydrates) while in high doses of OTA, different body systems are influenced like excretory, digestive, endocrine and circulatory system (Anzai *et al.*, 2010; Tinelli *et al.*, 2019).

In rodents, OTA caused effect on lymphoid organs such as enlarged kidneys and liver (Schwerdt *et al.*, 1999; Zlender *et al.*, 2009). Discharge of poison is finished by cylindrical emission and re-retention is guilty

of intra amassing of poison (Leier *et al.*, 2000; Jung *et al.*, 2001). Poison may be reabsorbed (from nephron) by dynamic vehicle and distant dispersion in pH.

Clinical Signs of Ochratoxins Toxicity in Poultry

The severity of clinical signs and symptoms of OTA toxicity depends upon the dose rate and the duration of exposure. The major signs exhibited by birds include general weakness, low FCR, stunted growth, poor egg and feathering quality, increased mortality, elevated weight of visceral organs like liver, spleen, pancreas, proventriculus, gizzard and testes in male birds (Resanovic, 2009). The kidney impairment leads to a decrease in urine concentration, glomerular filtration rate, impaired proximal tubule and degenerated ultrastructural changes in renal integrity (Elaroussi *et al.*, 2008). Day-old chicks when exposed to low dose of OTA, caused marked reduction in circulating lymphocytes in contrast to the enhanced ratio of monocytes and heterophils reported. This change in inflammatory cells profile in newly hatched day old chicks is ultimately related to their inflammation response against a variety of ecological pathogens and certainly disturbs their capability to react against vaccines (Moura *et al.*, 2004).

OTA along with nephrotoxicity also affects the liver and compromises the immune response, causing histopathological lesions in vital organs (Sharif *et al.*, 2018). OTA at 20mg/kg induces severe lesions in the glomerulus and convoluted tubules of the kidney. Interstitium incorporated with elevated levels of collagen fibers ultimately increases the membrane thickness. OTA also tempts abnormal mitochondria peroxisomes, lipid droplets inside the cytoplasm and nucleus, while the epithelium of convoluted tubules can be infiltrated with round electron-dense bodies, enhanced SER, intra-cytoplasmic and intra-nuclear myelin like projections (Sugiharto *et al.*, 2020). 400 and 800 µg level of OTA in poultry feed caused enlargement in renal and hepatic size along with ele-

vated levels of serum creatinine, uric acid, glutamic oxaloacetic transaminase, and glutamic pyruvic transaminase (Elaroussi *et al.*, 2008). In rabbits, teratogenic effects were found as skeleton abnormalities like incomplete ossification of ribs and skull bones, and soft tissues abnormalities due to OTA (Tinelli *et al.*, 2019).

Effect of Ochratoxin Biochemical & Histopathological Profile

Element of OTA remains beneath discussion and reported to be cancer-causing agent, toxic, immunotoxin and teratologic agent in poultry (Koszegi *et al.*, 2016). Elevated levels of ochratoxins ultimately causes adverse histopathological and biochemical changes along with reduced performance (Hassan *et al.*, 2010; Mohamed *et al.*, 2019). A high level of OTA showed a significant reduction ($p < 0.05$) in the antibody titers of anti-NDV by 10.4% and a non-significant reduction in mRNA cytokine IL-2 and IFR-gamma level upon induction of lipopolysaccharides. However, serum levels of these two parameters (IL-2 and interferon-gamma) significantly drop ($p < 0.05$) in the OTA toxin group. Anomalies in bursa, thymus, spleen, and liver with OTA+T-2 toxin and the use of commercially available mycofix Plus as treatment, encounter its toxic effects significantly (Xue *et al.*, 2010).

Moura *et al.* (2004) worked on different combination of OTA and PBS (Phosphate-buffered saline) to check effects of OTA on broilers leucocytes and reported that exposure of day old chicks to low doses of OTA resulted in a significant decline in proportion of circulating lymphocytes with a marked increase in proportion of monocytes and heterophils.

Indresh *et al.* (2013) observed the impacts of OTA upon the general performance, immunological and biochemical profile of broilers chicks. Both toxins caused dejecting effects on serum biochemical, hematological and immunological specifications, also affected health status of birds. Bharathi *et al.* (2014) assessed the changes in biochemical and liver antioxidant profile of birds by feeding of OTA at the rate of 100 ppb for 4 weeks. Results showed a prominent reduction in globulin level and IgA to IgG ratio in OTA fed birds. Moreover, hypo-glycaemia, hypo-amylasaemia, reduced high density lipids and elevated levels of ALT, ALP, and blood urea nitrogen, triglycerides were recorded. Thus, conclusively it was considered that 100 ppb OTA in feed results in severe damage to liver and kidneys along with causing adulterations in their normal biochemical and antioxidant profile.

Hassan *et al.* (2018) studied to investigate the prevalence of OTA in animal feed by using glutathione an antioxidant in rats. Using glutathione, an increase in urea, ALT, AST and decrease in serum total protein, albumin and globulin level was recorded in OTA treated rats. Results indicated the economic importance of glutathione by addition in healthy animal feed to overcome the deleterious effects of ochratoxins.

The suppression of the immune system and impairment of the normal physiology of several constituents of the immune system is also caused by OTA toxicity (Hassan *et al.*, 2012). A study affirmed the enhanced effects of bentonite clay in broiler chicks fed with aflatoxin and Ochratoxin treated feed by evaluating the pathological changes besides alterations in the immune system of treated birds. A depressed immune reaction in combination with pathological lesions in the immune system, reduced antibody (Ab) titer against sheep red blood cells, low response to PHA-P and impaired phagocytic activity was reported. The addition of bentonite clay in the aflatoxin group treated with 0.1 and 0.2 mg/kg dose rate exhibited an enriched response against immune-toxicity whereas no such prompt results were recorded in 0.6 mg/kg dose rate group. The OTA treated group showed only mild ameliorative effects upon bentonite clay addition in contrast to the aflatoxin group (Bhatti *et al.*, 2017). Histopathologic findings included vacuolation of hepatocytes, megakaryocytosis along with hyperplastic binary epithelial cell layer and increased liver weights. In kidneys, hypertrophied proximal tubule epithelial cell layer can be found beside a solidifying glomerulus basal membrane (Santin *et al.*, 2002). Pathological alterations induced by OTA are dependent on the duration of exposure and dose rate (Hameed *et al.*, 2013). The maximum acceptable level of OTA 0.1 mg OTA/kg was established by the European Commission considered as safe and no traces can be examined on breast and thigh muscles at this level. At 0.1 mg OTA/kg level no clinical sign and symptoms were examined because the dose level is less while mild histopathological lesions can be examined in such cases (Pozzo *et al.*, 2013). Liver and kidneys involvement in body's detoxification mechanism leads to hepato-renal enlargement, swollen and tan with white urate crystals in mild and complete failure with dehydration, hyper-uricemia in advanced OTA toxicity cases (Biró *et al.*, 2002).

Activity of Silymarin, Vitamin E and Absorbents against Ochratoxins

Different types of absorbents like Bentonite clay,

activated charcoal, distillery sludge, vitamin E, silymarin are used to control the activity of mycotoxins depending upon their mode of action. The use of vitamin E and selenium are beneficial to cope with the immunosuppressive effects of OTA. A study showed 11% gain in body weight caused by OTA but with less severe lesions in selenium and vitamin E treated birds (Ahmad *et al.*, 2012). 2% level of yeast sludge is more profitable in contrast to 1% and has safer zone against mycotoxins (Mujahid *et al.*, 2012). The effects of Ochratoxin A and its amelioration with silymarin and vitamin E in separate groups of white leghorn cockerels were tested. Hematological and serum biochemical parameters when evaluated in OTA treated birds showed diminish levels of PCV (packed cell volume), Hb. (hemoglobin), erythrocytic count, albumin, serum while increased levels of creatinine and urea as compared to vitamin E and silymarin treated groups (Ahmad *et al.*, 2012). Mycotoxin deactivator reduces the accumulation of ochratoxin in the organs while fecal excretion can be increased in such cases (Joo *et al.*, 2013).

Comparatively investigation of the 3 different adsorbents against Ochratoxin toxicity in birds show that the three different adsorbents effects on mycotoxin feed (a) esterified glucomannans, organic in nature, (b) modified zeolite of inorganic nature, and (c) combination of both glucomannan and zeolite. OTA treated groups and a combination of adsorbents show enhanced FCR and advanced histopathological changes in the kidney and liver. Organic and inorganic nature show high body weight and minimized

histopathological changes (Nedeljković-Trailović *et al.*, 2015). Unique sugar (STOC) termed as sucrose thermal oligosaccharide caramel on hematology, particular biochemical components, and hormones, fibro-nectin and cecal gram-negative bacterial levels affect the physiology. The addition of STOC in feed leads to improve the physiology of several parameters in exposure to OTA (Khaskheli *et al.*, 2020).

Abidin *et al.* (2013) focused on hematological and serum biochemical parameters in white Leghorn cockerels feeding OTA contaminated feed to study ameliorative effects of L-carnitine and vitamin E (α -tocopherol). Vitamin-E and L-carnitine alone or combination with OTA (1.0 mg/kg) can mitigate toxin produced hematological and serum biochemical specifications.

CONCLUSIONS

Conclusively, the presence of ochratoxins in poultry feed produces adverse effects on the poultry health and performance parameters. They also have immunosuppressive effects on birds. Ochratoxins also induce mild to moderate changes in the biochemical and histopathological profile. Wherever, the use of some adsorbents like bentonite, silymarin, and vitamin E proved to be effective against the adverse effects caused by OTA in birds and also improve performance parameters of birds.

CONFLICT OF INTEREST

None declared by the authors.

REFERENCES

- Ali AMA, Fahmy MF, Metwally MM, Hassanin O, Azazy HA, Mowafy RE (2020) Ameliorative effects of cholestyramine and oxihumate on aflatoxicosis in broiler chickens. *Pak Vet J* <http://dx.doi.org/10.29261/pakvetj/2020.093>.
- Abidin ZU, Khan M, Khatoon A, Saleemi MK, Khan A, Javed I (2013) Ameliorative effects of L-carnitine and vitamin E (α -tocopherol) on hematological and serum biochemical parameters in White Leghorn cockerels given ochratoxin A contaminated feed. *Br Poult Sci* 54:471-477.
- Ahmad MF, Saleemi MK, Khan MZ, Muhammad F, Khatoon A, Bhatti SA, Abbas RZ, Rizvi F, Ahmed I (2012) Effects of Ochratoxin A Feeding in White Leghorn Cockerels on Hematological and Serum Biochemical Parameters and its Amelioration with Silymarin and Vitamin E. *Pak Vet J* 32.
- Anzai N, Jutabha P, Endou H (2010) Molecular mechanism of Ochratoxin A transport in the kidney. *Toxins* 2: 1381-1398.
- Atef HA, El-Shafei HE, Mansour MK, Al-Kalamawy NM, El-Houda N, Hassan Y, Lashin AL (2018) Prevalence of Ochratoxigenic Fungi and Ochratoxin A Residues in Animal Feeds and Modulation of Their Toxic Effects by Glutathione. *Inter J Micr and App Sci* 7:2319-7706.
- Bhatti SA, Khan MZ, Saleemi MK, Saqib M, Khan A, Hassan ZU (2017) Protective role of bentonite against aflatoxin B1 and ochratoxin A-induced immunotoxicity in broilers. *J Immunotoxicol* 14:66-76.
- Bondy GS and Pestka JJ (2000) Immunomodulation by fungal toxins. *J Toxicol Environ Health B Crit Rev* 3:109-143.
- Bui-Klimke T and Wu F (2014) Evaluating weight of evidence in the mystery of balkan endemic nephropathy. *Risk Anal* 34:1688-1705.
- Berger V, Gabriel AF, Sergent T, Trouet A, Larondelle Y, Schneider YJ, (2003) Interaction of Ochratoxin A with human intestinal Caco-2 cells: Possible implication of a multidrug resistance-associated protein (MRP2). *Toxicological Letters* 140-141, 465-476.
- Bharathi R, Pazhanivel N, Balachandran C, Dhinakar RG (2014) Effect of dietary ochratoxin on biochemical and antioxidant profile in broiler chickens. *I J Poult Sci* 49: 331-333.
- Baran A, Adigüzel MC, Yüksel M (2020) Prevalence of antibiotic-resistant and extended-spectrum beta-lactamase-producing *Escherichia coli* in chicken meat from Eastern Turkey. *Pak Vet J* 40: 355-359.
- Biró K, Solti L, Barna-Vetró I, Bagó G, Glávits R, Szabó E, Fink-Gremmels J (2002) Tissue distribution of ochratoxin A as determined by HPLC and ELISA and histopathological effects in chickens. *Avian Pathol* 31: 141-148. <https://doi.org/10.1080/03079450120118621>
- Carmen S, Coman I, Solcan Gh, Miron L, Oprean OZ (2008) Histological and ultrastructural lesions of the kidney in experimental ochratoxicosis of broiler chickens. *Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca. Veteri Medic* 65.
- Elmossalamy DA, Hamdy MM, Aideia HAM, Yassien NA, Zaki HMBA, 2020. Incidence of *Staphylococcus aureus* and its enterotoxins in chicken meat and its products. *Int J Vet Sci* 9: 573-577.
- Fortza N, Negoescu M (1961) Nefrita cronica azotemica endo-epidemică, *CercetMed* 1:217-221.
- Ghonaim MIE, Eid AM, Elmossalami MK, Abdel-Naeem HHS (2020) Sensory, deterioration and bacteriological assessment of some ready to eat

- poultry products. *Int J Vet Sci* 9: 568-572.
- Gohar UF, Mukhtar H, Mushtaq A, Farooq A, Saleem F, Hussain MA and Ghani MU (2020) Fungi: A potential source of biopharmaceuticals. *Agrobiol Records* 2: 49-62. <https://doi.org/10.47278/journal.abr/2020.013>
- Hagelberg S, Hult K, Fuchs R (1989) Toxicokinetics of Ochratoxin A in several species and its plasma-binding properties. *J Appl Toxicol* 9:91-96.
- Hameed MR, Khan MZ, Khan A, Javed I (2013) Ochratoxin induced pathological alterations in broiler chicks: effect of dose and duration. *Pak Vet J* 33:145-149.
- Hassan ZU, Khan MZ, Saleemi MK, Khan A, Javed I, Noreen M (2012) Immunological responses of male White Leghorn chicks kept on ochratoxin A (OTA)-contaminated feed. *J. Immunotoxicol.* 9:56-63.
- Hassan ZU, Saleemi KM, Khan A, Javed I (2010) Pathological responses of White Leghorn breeder hens kept on ochratoxin A contaminated feed. *Pak Vet J* 30:118-123
- Hassan ZU, Thania R, Atiab FA, Meerb SA, Mighelic Q, Jaoua S (2018) Co-occurrence of mycotoxins in commercial formula milk and cereal-based baby food on the Qatar market. *FOOD Addi & Conta* 11:191-197. <https://doi.org/10.1080/19393210.2018.1437785>
- Imran M, Cao S, Wan SF, Chen Z, Saleemi MK, Wang N, Naseem MN and Munawar J (2020) Mycotoxins- A global one health concern: A review. *Agrobiol Records* 2: 1-16.
- Indresh HC and Umakantha B (2013) Effects of ochratoxin and T-2 toxin combination on performance, biochemical and immune status of commercial broilers. *Vet World* 6: 945-949.
- Ismail AA and Papenbrock J (2015) Mycotoxins: Producing Fungi and Mechanisms of Phytotoxicity. *Agriculture* 5:492-537.
- Joint FAO/WHO (2001) Safety evaluation of certain mycotoxins in food. In: Prepared by the 56th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series L: 46. Ochratoxin A. International Programme on Food Safety. Geneva: World Health Organization, 281-415.
- Jarvis BB and Miller JD (2005) Mycotoxins as harmful indoor air contaminants. *Appl. Microbiol. Biotechnol.* 66:367-372.
- Joint F, W.E.C.o.F. Additives and W.H. Organization (2002) Evaluation of certain mycotoxins in food: fifty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization.
- Joo YD, Kang CW, An BK, Ahn JS, Borutova R (2013) Effects of ochratoxin A and preventive action of a mycotoxin-deactivation product in broiler chickens. *Veterin zoot* 61:22-29.
- Jung KY, Takeda M, Kyung Kim D, Tojo A, Narikawa S, Yoo BS, Hosoyamada M, Cha SH, Sekine T, Endo H (2001) Characterization of Ochratoxin A transport by human organic anion transporters. *Life Sci* 69: 2123-2135.
- Khater HF, Ziam H, Abbas A, Abbas RZ, Raza MA, Hussain K, Younis EZ, Radwan IT, Selim A (2020) Avian Coccidiosis: Recent Advances in Alternative Control Strategies and Vaccine Development. *Agrobiol Records* 1: 11-25.
- Khaskheli AA, MI Khaskheli, AJ Khaskheli and AA Khaskheli (2020) Dietary influence of *Yuccaschidigera* on broilers and layers: a review. *Int J Vet Sci* 9: 458-461.
- Khatoon A, Khan MZ, Khan A, Javed I (2016) Toxicopathological and serum biochemical alterations induced by ochratoxin A in broiler chicks and their amelioration by locally available bentonite clay. *P J AgriSci* 53:977-84.
- Khatoon A, Khan MZ, Abidin ZU, Khan A, Saleemi MK (2017) Mitigation potential of distillery sludge against ochratoxin A induced immunological alterations in broiler chicks. *World Myco J* 10: 255-262.
- Ko'szegi T and Poór M (2016) Ochratoxin A: Molecular Interactions, Mechanisms of Toxicity and Prevention at the Molecular Level. Review paper toxins, 2-12.
- Kemboi DC, Ochieng PE, Antonissen G, Croubels S, Scippo ML, Okoth S, Gathumbi JK (2020) Multi-Mycotoxin Occurrence in Dairy Cattle and Poultry Feeds and Feed Ingredients from Machakos Town, Kenya. *Toxins* 12: 762.
- Lin X, Mohsin M, Abbas RZ, Li L, Chen H, Huang C, Li Y, Goraya MU, Huang Z and Yin G, 2020. Evaluation of immunogenicity and protective efficacy of *Eimeria maxima* immune mapped protein 1 with EDA adjuvant in chicken. *Pak Vet J* 40: 209-213.
- Lino CM, Baeta ML, Henri M, Dinis AMP, Pena AS, Silveira MIN (2008) Levels of Ochratoxin A in serum from urban and rural Portuguese populations and estimation of exposure degree. *Food and Chem Toxicol* 46: 879-885.
- Leier I, Hummel-Eisenbeiss J, Cui Y, Keppler D (2000) ATP-dependent para-aminohippurate transport by apical multidrug resistance protein MRP2. *Kidney International*, 57: 1636-1642.
- Mohamed MY, AM AEH, Ibrahim EMM, Abd El, Mola AM (2019) Ameliorating effects of organic and inorganic mycotoxin binders on the performance of Ossimi sheep. *Egyptian J Sheep and Goats Sci* 14: 33-48.
- Marquardt RR and Frohlich AA (1992) A review of recent advances in understanding ochratoxicosis. *J. Anim. Sci.* 70:3968-3988.
- Moss M (1996) Mode of formation of ochratoxin A. *Food Addit. Contam.* 13:5-9.
- Moussa AI, Sobeih AMK, Al-Hawary II, Elkassas WM and Barakat R, 2020. Efficacy of kaolin and bentonite clay to reduce aflatoxin M1 content in contaminated milk and effects on milk quality. *Pak Vet J* <http://dx.doi.org/10.29261/pakvetj/2020.001>
- Moura MC, Machado L, Porfirio LC, Freire RB (2004) Effects of ochratoxin A on broiler leukocytes. *Brazilian J Poul Sci* 6:187-190.
- Mujahid H, Hashmi AS, Anjum AA, Waris A, Tipu A (2012) Detoxification potential of ochratoxin by yeast sludge and evaluation in broiler chicks. *J Anim Plant Sci.* 22:601-604.
- Nedeljković-Trailović J, Trailović S, Resanović R, Milićević D, Jovanović M, Vasiljević M (2015) Comparative investigation of the efficacy of three different adsorbents against OTA-induced toxicity in broiler chickens. *Toxins (Basel).* 7:1174-1191.
- Pozzo L, Cavallarin L, Antoniazzi S, Guerre P, Biasibetti E, Capucchio MT, Schiavone A (2013) Feeding a diet contaminated with ochratoxin A for broiler chickens at the maximum level recommended by the EU for poultry feeds (0.1 mg/kg). 2. Effects on meat quality, oxidative stress, residues and histological traits. *J. Anim. Physiol. Anim. Nutr* 97:23-31.
- Pohland AE, Schuller PL, Steyn PS (1982) Physicochemical data for some selected mycotoxins. *Pure Appl. Chem* 54: 2219-2284.
- Pohland AE, Nesheim S, Friedman L (1992) Ochratoxin A: A review. *Pure Appl. Chem* 64:1029-1046.
- Poór M, Kuzma M, Matisz G, Li Y, Czibulya Z, Peles-Lemli B, Ko'szegi T (2013) Interaction of alkali and alkaline earth ions with Ochratoxin A. *J. Lumin* 135: 276-280.
- Roth A, Chakor K, Creppy EE, Kane A, Rosenthaler R, Dirheimer G (1988) Evidence for an enterohepatic circulation of Ochratoxin A in mice. *Toxicol* 48:293-308.
- Santin E, Paulillo AC, Maiorka PC, Alessi AC, Krabbe EL, Maiorka A (2002) The effects of ochratoxin/aluminosilicate interaction on the tissues and humoral immune response of broilers. *Avian Pathol* 31:73-79.
- Schleibinger H, Keller R, Rüdén H (2004) Indoor air pollution by microorganisms and their metabolites. In: *Air Pollution*. Springer 149-177.
- Sharif M, Shoaib M, Rahman MZ, Ahmad F, Rehman SU (2018) Effect of distillery yeast sludge on growth performance, nutrient digestibility and slaughter parameters in Japanese quails. *Scien Repor.*
- Shoaib M, Riaz A, Hassan MU, Yousaf A, Rehman SU, Zafar MA, Kamran M, Amir RM, Malik AM (2020) Sero-prevalence and associated risk factors of *Mycoplasma Gallisepticum*, *Mycoplasma Synoviae*, *Salmonella Pullorum* / *Gallinarum* in poultry. *Pak Vet J* 40: 253-256
- Schwerdt G, Freudinger R, Silbernagl S, Gekle M (1999) Ochratoxin A—binding proteins in rat organs and plasma and in different cell lines of the kidney. *Toxicol* 135: 1-10.
- Sugiharto S, E Widiastuti, I Isroli, T Yudiarti, TA Sartono, HI Wahyuni (2020) Physical and chemical characteristics of meats of the Indonesian indigenous crossbred chickens fed fermented mixture of papaya (*Carica papaya* L.) leaf and seed meal. *Int J Vet Sci* 9: 462-465.
- Tinelli A, Passantino G, Perillo A, Zizzo N (2019) Anatomopathological consequences of mycotoxins contamination in rabbits feed. *Iranian J Appl Anim Sci.* 9: 379-387.
- Trivedi AB, Doi E, Kitabatake N (1992) Detoxification of Ochratoxin A on heating under acidic and alkaline conditions. *Biosci Biotechnol Biochem* 56:741-745.
- Vieira SL (2003) Nutritional implication of Mold development in feed stuffs and alternative to reduce the mycotoxins problem in poultry feeds. *World Poult Sci J*, 59:111-122.
- Wang Y, Lu G, Chai T (2006) Quantitative evaluation for the potential harm of fungal aerosol in chicken house. *Acta Ecol. Animalis Domasti* 27:34-41.
- Xue CY, Wang GH, Chen F, Zhang B, Bi YZ, Cao YC (2010) Immunopathological effects of ochratoxin A and T-2 toxin combination on broilers. *Poult Sci* 89:1162-1166.
- Yasmin S, Nawaz M, Anjum AA, Ashraf K, Basra MAR, Mehmood A, Khan I, Malik F, 2020. Phytochemical analysis and *In Vitro* activity of essential oils of selected plants against *Salmonella enteritidis* and *Salmonella gallinarum* of poultry origin. *Pak Vet J* 40: 139-144.
- Žlender V, Breljak D, Ljubojević M, Flajs D, Balen D, Brzica H, Domijan AM, Peraica M, Fuchs R, Anzai N, Sabolić I (2009) Low doses of Ochratoxin A upregulate the protein expression of organic anion transporters Oat1, Oat2, Oat3 and Oat5 in rat kidney cortex. *Toxicol Appl Pharmacol* 239: 284-296.
- Zhang K, Li X, Na C, Abbas A, Abbas RZ and Zaman MA (2020) Anticoccidial effects of *Camellia sinensis* (green tea) extract and its effect on Blood and Serum chemistry of broiler chickens. *Pak Vet J* 40: 77-80.