

Letter to Editor

Inhalation toxicity of mycotoxins in farm animals

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Dear Editor,

Mycotoxins contamination in animal feed is increasingly becoming unavoidable worldwide. They can subsequently threaten global public health. Various studies have signified their carcinogenic effects, and damage to the gastrointestinal tract, liver, and kidneys and other organs (Gallo *et al.*, 2015; Alshannaq and Yu, 2017). Although ingestion is known as the most common route of mycotoxins exposure, dermal contact, and inhalation have been established, particularly for agricultural workers, handling mycotoxins contaminated feed. Association between inhalation of mycotoxins and systemic pathology such as kidney disease have been shown previously (Hope and Hope, 2012), but very few kinds of literature are available. Due to the low molecular weights of mycotoxins (Janik *et al.*, 2020), they can easily be aerosolized. Substantiating this, dust samples from grain processing facilities were positive for the presence of *Aspergillus flavus* and mycotoxins aflatoxins (Ghosh *et al.*, 1997; Sales and Yoshizawa, 2006). Further, dust and aerosol samples collected from cowsheds, poultry sheds, and animal housing contained ochratoxin-A (OTA) along with aflatoxin and zearalenone (Richard *et al.*, 1999; Skaug *et al.*, 2001; Wang *et al.*, 2008).

Mycotoxins from contaminated roughage or grains may also be inhaled and injure domestic animals. Although the toxicity of mycotoxins via ingestion has been well documented, very few authors have demonstrated the adverse effects of mycotoxins on respiratory system. A recent experiment indicated the mediated damage of aflatoxins from occupational environments on respiratory epithelial cells (Jaksic *et al.*, 2019). Further, *in-vitro* and *ex-vivo* studies have showed disruption the integrity and barrier function of respiratory epithelial cells by mycotoxin deoxynivalenol (DON) in horses; these injured equine respiratory cells were further predisposed to equine herpes virus (EHV1) infection (Van Cleemput *et al.*, 2019). In another study, aflatoxins

impaired ciliary beat frequency, consequently hampering respiratory physical defences against inhaled pathogens (Lee *et al.*, 2016). Additionally, it was shown that mycotoxins could directly enhance the replication of respiratory pathogens (porcine circo virus) in the respiratory epithelium (Gan *et al.*, 2015). In-fact, such increased infection by pathogens after exposure to mycotoxins is not restricted to respiratory system and noticed in other tissues such as gastrointestinal tract. For example, following exposure to fusarium mycotoxins epithelial damage and enhanced intestinal epithelial invasion, colonization and translocation by pathogenic bacteria (*E. coli*, *Salmonella*) were seen in many species including pigs, cattle, and poultry (Oswald *et al.*, 2003; Antonissen *et al.*, 2014). Thus providing a similar plausible mechanistic link between mycotoxin exposure and bacterial or viral pathogenesis in respiratory system. Moreover, immunotoxic effects of mycotoxins have been shown to cause allergic airway disorders, pneumonia, and chronic pulmonary disease both in animals and humans through either immunosuppression or over stimulation (Schütze *et al.*, 2010; Cai *et al.*, 2011; Park *et al.*, 2015). While the diverse composition of aerosols poses a challenge for investigating the health risk of inhaled mycotoxins, the same diversity could contribute to enhanced toxic effects of mycotoxins such as increased toxicity of mycotoxin DON in inducing pro-inflammatory response in presence of pathogens (Gu *et al.*, 2021).

The above arguments emphasize the need for research on inhalation hazard of mycotoxins. But to date, a lot is unknown in terms of toxicity of inhaled mycotoxins on different species, age, and sex of animals. Given the nature of work in agricultural scenario, even when the levels of mycotoxins in feed are below maximum permissible limits, long-term exposure to low dose of inhaled mycotoxins is of concern in animals. Thus, the current article is written to motivate research community to address the gap in work on inhaled mycotoxins that in-turn could aid in mycotoxin

mitigation strategies.

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Conflict of interest

We declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

References

- Alshannaq, A and Yu, JH** (2017). Occurrence, toxicity, and analysis of major mycotoxins in food. *Int. J. Environ. Res. Public Health.*, 14: 1-20. <https://doi.org/10.3390/ijerph14060632>.
- Antonissen, G; Martel, A; Pasmans, F; Ducatelle, R; Verbrugge, E; Vandebroucke, V and Croubels, S** (2014). The impact of *Fusarium* Mycotoxins on human and animal host susceptibility to infectious diseases. *Toxins.*, 6: 430-452. <https://doi.org/10.3390/toxins6020430>.
- Cai, GH; Hashim, JH; Hashim, Z; Ali, F; Bloom, E; Larsson, L and Norbäck, D** (2011). Fungal DNA, allergens, mycotoxins and associations with asthmatic symptoms among pupils in schools from Johor Bahru, Malaysia. *Pediatr. Allergy Immuno.*, 22: 290-297. <https://doi.org/10.1111/j.1399-3038.2010.01127.x>.
- Gallo, A; Giuberti, G; Frisvad, JC; Bertuzzi, T and Nielsen, KF** (2015). Review on mycotoxin issues in ruminants: Occurrence in forages, effects of mycotoxin ingestion on health status and animal performance and practical strategies to counteract their negative effects. *Toxins.* 7: 3057-3111. <https://doi.org/10.3390/toxins7083057>.
- Gan, F; Zhang, Z; Hu, Z; Hesketh, J; Xue, H; Chen, X and Huang, K** (2015). Ochratoxin A promotes porcine circovirus type 2 replication *in vitro* and *in vivo*. *Free Radic. Biol. Med.*, 80: 33-47.
- Ghosh, SK; Desai, MR; Pandya, GL and Venkaiah, K** (1997). Airborne aflatoxin in the grain processing industries in India. *Am. Ind. Hyg. Assoc. J.*, 58: 583-586. <https://doi.org/10.1080/15428119791012513>.
- Gu, C; Gao, X; Guo, D; Wang, J; Wu, Q; Nepovimova, E and Kuca, K** (2021). Combined effect of deoxynivalenol (DON) and porcine circovirus type 2 (Pcv2) on inflammatory cytokine mRNA expression. *Toxins*, 13: 1-15.
- Hope, JH and Hope, BE** (2012). A review of the diagnosis and treatment of ochratoxin a inhalational exposure associated with human illness and kidney disease including focal segmental glomerulosclerosis. *J. Environ. Public Health.*, 2012: 1-12. <https://doi.org/10.1155/2012/835059>.
- Jaksic, D; Kocsubé, S; Bencsik, O; Keckeméti, A; Szekeres, A; Jelic, D and Klarić, MŠ** (2019). Aflatoxin production and *in vitro* toxicity of *Aspergilli* section *Flavi* isolated from air samples collected from different environments. *Mycotoxin Res.*, 35: 217-230.
- Janik, E; Niemcewicz, M; Ceremuga, M; Stela, M; Saluk-bijak, J; Siadkowski, A and Bijak, M** (2020). Molecular aspects of mycotoxins—A serious problem for human health. *Int. J. Mol. Sci.*, 21: 1-21.
- Lee, RN; Workmand, AD; Carey, RM; Chen, B; Rosen, PL; Doghramji, L and Cohen, NA** (2016). Fungal aflatoxins reduce respiratory mucosal ciliary function. *Sci. Rep.*, 6: 1-13. <https://doi.org/10.1038/srep33221>.
- Oswald, IP; Desautels, C; Laffitte, J; Fournout, S; Peres, SY; Odin, M and Fairbrother, JM** (2003). Mycotoxin fumonisin B1 increases intestinal colonization by pathogenic *Escherichia coli* in pigs. *Appl. Environ. Microbiol.*, 69: 5870-5874. <https://doi.org/10.1128/AEM.69.10.5870-5874.2003>.
- Park, SH; Kim, D; Kim, J and Moon, Y** (2015). Effects of mycotoxins on mucosal microbial infection and related pathogenesis. *Toxins*, 7: 4484-4502. <https://doi.org/10.3390/toxins7114484>.
- Richard, JL; Plattner, RD; May, J and Liska, SL** (1999). The occurrence of ochratoxin A in dust collected from a problem household. *Mycopathologia.*, 146: 99-103. <https://doi.org/10.1023/A:1007056627296>.
- Sales, A and Yoshizawa, T** (2006). *Aspergillus* section *Flavi* and aflatoxins in dusts generated by agricultural processing facilities in the Philippines. *J. Sci. Food Agric.*, 86: 2534-2542. <https://doi.org/10.1002/jsfa>.
- Schütze, N; Lehmann, I; Bönisch, U; Simon, JC and Polte, T** (2010). Exposure to mycotoxins increases the allergic immune response in a murine asthma model. *Am. J. Respir. Crit. Care Med.*, 181: 1188-1199. <https://doi.org/10.1164/rccm.200909-1350OC>.
- Skaug, MA; Eduard, W and Størmer, FC** (2001). Ochratoxin A in airborne dust and fungal conidia. *Mycopathologia.*, 151: 93-98. <https://doi.org/10.1023/A:1010953401173>.
- Van Cleemput, J; Poelaert, KCK; Laval, K; Van den Broeck, W and Nauwynck, HJ** (2019). Deoxynivalenol, but not fumonisin B1, aflatoxin B1 or diesel exhaust particles disrupt integrity of the horse's respiratory epithelium and predispose it for equine herpesvirus type 1 infection. *Vet. Microbiol.*, 234: 17-24. <https://doi.org/10.1016/j.vetmic.2019.05.009>.
- Wang, Y; Chai, T; Lu, G; Quan, C; Duan, H; Yao, M and Schlenker, G** (2008). Simultaneous detection of airborne Aflatoxin, Ochratoxin and Zearalenone in a poultry house by immunoaffinity clean-up and high-performance liquid chromatography. *Environ. Res.*, 107: 139-144. <https://doi.org/10.1016/j.envres.2008.01.008>.