Mycoxotins: A gateway

Mycotoxins may alter animals’ susceptibility to infectious diseases by affecting intestinal health and the innate and adaptive immune system.

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Mycotoxins are structurally diverse secondary metabolites produced by fungi that contaminate feedstuffs consumed by animals. Consumption of some mycotoxins, at levels that do not cause overt clinical mycotoxicosis, suppress immune functions and may decrease resistance to infectious disease. The systemic effect of the immune system to mycotoxin-induced immunosuppression arises from the vulnerability of the highly proliferating and differentiating cell types involved in the immune-mediated activities and regulate the complex communication network between cellular and humoral components. Mycotoxin-induced immunosuppression may be expressed as depressed T or B lymphocyte activity, suppressed immunoglobulin and antibody production, reduced complement or interferon activity or impaired macrophage-effector cell function. Although the mode of action of many specific immunosuppressive effects of mycotoxins are presently unclear, inhibition of DNA, RNA and protein synthesis via a variety of different mechanisms appears to be either directly or indirectly responsible for the immunosuppressive action of many mycotoxins.

Intestinal tract immunity

Deoxynivalenol (DON) is a mycotoxin produced by Fusarium spp. that belongs to trichothecene mycotoxins. Among the mycotoxins that affect swine are the most susceptible to DON as it markedly reduces feed intake and decreases weight gain. DON has also been shown to increase susceptibility to viral infections (Saward et al., 2014).

The economic costs of mycotoxins are impossible to determine accurately (Wu et al., 2008), but the Food & Drug Administration estimated that in the U.S., the mean economic annual cost of crop losses from the mycotoxins, fumonisins and DON is $932 million (Council for Agricultural Science & Technology, 2003).

The intestinal mucosa acts as a barrier to prevent the entry of foreign antigens into the body via food, sensory, drugs, toxins, commensal microbiota and pathogenic agents — into the underlying tissues (Bouhet and Oswald, 2005). Although the mode of action of many specific immunosuppressive effects of mycotoxins are presently unclear, inhibition of DNA, RNA and protein synthesis via a variety of different mechanisms appears to be either directly or indirectly responsible for the immunosuppressive action of many mycotoxins.

Important components of the innate immune system are the intestinal epithelial cells, which are interconnected by tight junctions and covered with mucus produced by goblet cells (Schunk and Mueller, 2006). Several studies indicate that DON is able to increase the permeability of the porcine intestinal epithelial layer (Pinston et al., 2009) and affect the viability and proliferation of porcine intestinal epithelial cells (Yum et al., 2012).

Several mycotoxins are also able to modulate the production of cytokines, while DON increases the expression of tumor-like growth factor-beta and interferon-gamma in intestinal epithelial cells (Bouhet and Oswald, 2005).

At the cellular level, the main toxic effect of DON appears to be a primary inhibition of protein synthesis, followed by disruption of DNA and RNA synthesis. DON affects actively dividing cells, as those lining the gastrointestinal tract. It should be noted that the gastrointestinal tract is also sensitive to DON-induced apoptosis, since that changes the gastric mucosal, gastric granular epithelium and intestinal crypt cell epithelium (Bonyd and Peskova, 2008).

Viruses more effective

Fusarium mycotoxins, including DON, negatively affect the internal reovirus clearance. Li et al. (2006) showed that DON and T-2 suppress the host immune response to reovirus, as evidenced by the inability to clear the virus from the intestine as well as by increased fecal shedding of the virus.

Trichothecene exposure increases the intestinal viral load, which could increase inflammation and discomfort to the host during the infection process. The increased fecal shedding could enhance virus dissemination among individuals (Li et al., 2006). These results could imply that mycotoxins affect host susceptibility to more virulent and aggressive viruses such as porcine reproductive and respiratory syndrome virus (PRRSV), porcine circovirus-2 (PCV2) or porcine epidemic diarrhea virus (PEDV).

PRRSV is a highly infectious virus that replicates within the monocytes or macrophages, with the lungs being a predominant site of viral multiplication (Ramos et al., 2010). Exposure of piglets to the Fusarium mycotoxin fumonisin B1 (FB1) increased the risk for PPRSV disease (Bane et al., 1997). More severe histopathological lesions were observed when pigs were exposed to FB1 and were subsequently inoculated with PPRSV. The authors suggested that FB1 causes immunosuppression, facilitating PPRSV to induce more severe lesions (Ramos et al., 2010).

PEDV pathogenesis and immune mechanisms are similar to those reported for transmissible gastroenteritis (TGE). Oral infection results in viral replication in the epithelial cells of the small intestinal villi. Cells on colonic villi also may become infected. On large farming breeds, the virus persists in the presence of litters of pigs after weaning and after they lose their immunity from antibodies in the sow’s milk. On these farms, PEDV may be associated with weaning diarrhea.

The integrity of the gut is dependent on the maintenance of various factors, including enterocyte and mucus layer integrity, as well as the preservation and functionality of epithelial junctions cells (Randal et al., 2011).

There is increasing evidence that the intestinal epithelium can be directly exposed to mycotoxins, and at a higher concentration than other tissues (Greenwell et al., 2013). The ingestion of mycotoxins may induce changes in intestinal morphology and local immunity (Iracaren et al., 2012), affect the barrier function of the gut and, finally, open the door for viral infections such as PEDV or TGE.

Given the importance of mycotoxins in worldwide swine production and the frequent occurrence of different mycotoxins, including DON, more detailed research should be performed to investigate their interaction.

The important role of mycotoxins should be highlighted in the etiology of such disease as porcine ear necrosis syndrome (PEN), which is the most common isolated agent in lesions of PENS cases, but other pathogens such as Mycoplasma su坦, Streptococcus suis and spirochetes are often implicated (Thacker, 2006).

Moreover, non-infectious factors such as intensive pen density and overcrowded, poor air quality with high concentrations of gases (e.g., ammonia), poor hygienic conditions, copper and magnesium deficiency and cannibalism were associated with an increased risk of PENS (Busch et al., 2008).

Recently, an important causative role has also been attributed to immunosuppressive agents such as PCV2 and PRRSV, as well as mycotoxins (Allan and Ellis, 2000).

Summary

In summary, mycotoxins may alter animals’ susceptibility to infectious diseases by affecting intestinal health and the innate and adaptive immune system. Further research will be necessary to investigate the effects of mycotoxins on infectious diseases and to develop practical, economically justified solutions to counteract mycotoxin contamination of feed and its effects on animal health.

References