

Mycotoxins and immunity

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1. General effects

Generally, two different mechanisms are involved in the immune response: **innate immune response** (nonspecific, fast, activation of phagocytes such as macrophages and neutrophils, secretion of cytokines, prostaglandins and reactive oxygen and nitrogen species) and **acquired immune response** (specific, memory, lymphocytes, B-cell humoral response with antibodies and T-cell cellular response with cytokines and cytotoxicity).

→ Mycotoxins can interact on all different levels of the immune response. The complex cascade of effects can already be initiated at low doses.

1.1. Mycotoxins and inflammation

Aflatoxins, ochratoxins, fumonisins (FB) and patulin have immunomodulatory properties and therefore alter the inflammatory response. They can *inter alia* impact the viability and functionality/production of cytokines of macrophages and neutrophils.

1.2. Mycotoxins and humoral immune response

Deoxynivalenol (DON) is known to cause an elevation of IgA in serum and a concomitant depression of IgM and IgG in mice. In pigs, only the increase of IgA is observed.

1.3. Mycotoxins and Cellular response

Aflatoxin B1 (AFB1) is the most studied mycotoxin in combination with the cellular immune response. In chickens, AFB1 suppresses the cell mediated immune response. The general mechanism for the immunosuppressive effects of AFB1 are directly related to the impaired protein synthesis in chickens. AFB1 is transformed in vivo into active metabolites that bind to DNA and RNA, impairs DNA-dependent RNA polymerase activity and inhibits RNA and protein synthesis. Inhibition of DNA, RNA and protein synthesis directly and indirectly affects the proliferation and differentiation of cells of the lymphoid system, and the synthesis of cytokines that regulate the communication network of the immune system.

2. Main effect of the mycotoxins on the immune response

2.1. Aflatoxins

Aflatoxins influence the innate as well as the acquired immune response.

Cell-mediated immunity

- Dysregulation of the antigen-presenting properties of dendritic cells.
- T-cell proliferation by dendritic cells is induced → presenting capacity enhanced

Inflammation/innate immunity

- Reduced synthesis of pro-inflammatory cytokines and increase of anti-inflammatory cytokines
- Alteration of macrophages and neutrophils in utero

Humoral immunity

- No influence on humoral immune response after vaccination

2.2. Trichothecenes

The trichothecenes, such as DON and T-2 toxin (T-2) can have immune stimulatory or inhibitory effects.

Inflammation/innate immunity

- Disrupting intracellular signalling with leukocytes → dose dependent effect
 - Low dose → stimulatory effect
 - High dose → inhibitory effect
- Influencing the ribosome: activating MAPKs → positive effect on the immune system
- Reduction in neutrophil phagocytosis in ruminants and macrophage phagocytosis in swine
- Chronic DON exposure in chickens → lowering TNF-α

Acquired immune response

- Increase of IgA in serum
- Increase (DON) or decrease (T2) of anti-IgG in serum
- High doses T2 → decrease of mitogenic/antigenic-specific lymphocyte proliferation
- Reduction of white blood cells and total lymphocytes numbers in laying hens

2.3. Fumonisin

Acquired immune response

- Impair Th1/Th2 cytokine balance & impaired humoral response
- Reduction of antigen specific titer in male pigs after mycoplasma vaccination
- No effects on IgA, IgG and IgM
- Impairs maturation of antigen-presenting cells.

Inflammation

- Cell death of alveolar macrophages
- Decrease of IL-6 and IL-1β in spleen tissue

2.4. Ochratoxin A (OTA)

- Reduced and delayed hypersensitivity to tuberculin and phytohemagglutinin
- Reduced lymphoblastogenesis
- Reduced phagocytosis activity
- Impact on cytokine expression

2.5. Zearalenone

The effect of zearalenone (ZEN) on the immune response in animals has not been extensively studied so far. However, some immunomodulation effect are known:

- Increased synthesis of IL-8 and IL-10 after exposure to intestinal epithelial cells
- Chronic inflammation in the intestines of sows

3. Significance for the animals

In pigs, the level of mycotoxins will often not be high enough to show direct toxic effects/disease but through their immunomodulatory effects, these mycotoxins can reduce the performance of the animals and consequently lead to economic losses.

3.1. Susceptible for infectious diseases

In general the effects of mycotoxins on the immune system lead to a decrease of the animals' resistance to infections or increase the susceptibility of the animals to infectious diseases.



Poultry

T2 toxin	Increased susceptibility to infections by <i>Salmonella</i> species and <i>Cryptosporidium bailey</i>
AFB1	Increased severity of coccidiosis and salmonellosis
OTA	Increased susceptibility to coccidiosis, salmonellosis, colibacillosis



Pigs

AFB1	Increased severity of <i>Erysipelothrix rhusiopathiae</i> and <i>Brachyspira hyodysenteriae</i> infections
OTA	Increased susceptibility for <i>Salmonella choleraesuis</i> , <i>Serpulina hyodysenteriae</i> , <i>Campylobacter coli</i> , <i>Brachyspira hyodysenteriae</i> + PSV2 → increases viremia in serum
FB1	Increased susceptibility for <i>Escherichia coli</i> /intestinal infections and pulmonary infections Increased severity of pathological changes after bacterial/viral infections
DON	+ PCV2 → viral infection increases + PRRSV → increased infection, more lesions + Bacterial infections → enhances the inflammatory response IgA increases, thus also more resistant against certain pathogens

3.2. Vaccination

Immunity acquired through vaccination is also impaired by mycotoxin ingestion. The mycotoxin dose that alters the vaccine immune response is lower than the one that alters the global immune response.

AFB1	Erysipelas vaccination in swine impaired Fowl cholera and Marek's disease in poultry (no influence on Newcastle disease in poultry)
FB1	Decreases antibody response during vaccination
AFB1 and T2	Reduce vaccine response to OVA-vaccination
DON	Inhibits efficiency of vaccination against PRRSV-modified live vaccine. Inhibits efficiency of IBV and Newcastle disease vaccination in poultry.

3.3. Drug efficacy

T-2 toxin reduces the anticoccidial efficacy of lasalocid in chickens.

The information in this technical bulletin is based on the content of following references.

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3. Awad, W., Ghareeb, K., Böhm, J. & Zentek, J. The Toxicological Impacts of the *Fusarium* mycotoxin, Deoxynivalenol, in Poultry Flocks with Special Reference to Immunotoxicity. *Toxins (Basel)* 5, 912–925 (2013).