Review of interaction of mycotoxins and endotoxins on inflammatory response

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Introduction

An effective immune system is determining for animal health and well being. Commercial animal production is based on balanced feed providing required nutrients and optimized environment. However, some stresses are difficult to avoid and are responsible for immune suppression, increased susceptibility to diseases and consequently decreased productivity of farm animals. Mycotoxins are one of the most immunosuppressive factors in animal diets (Surai and Drovska, 2005) even at levels that do not cause overt clinical mycotoxicosis (Corrier, 1991). Deoxynivalenol (DON) is one of the most common *Fusarium* trichothecene mycotoxins (Schothorst and van Egmond, 2004). Like other trichothecenes, DON induces a spectrum of effects. The purpose of this paper is to describe the influence of DON and endotoxins on inflammatory response.

1. Impact of DON on inflammatory response

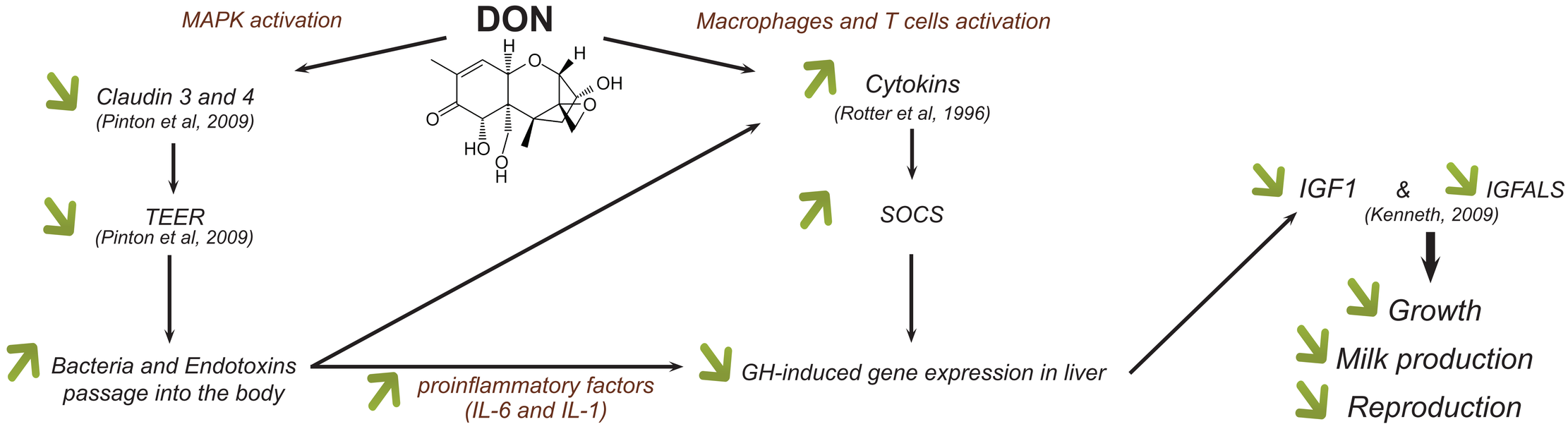


Chart 1: DON impact on inflammatory response

(MAPK: Mitogen-activated protein kinases; TEER : Trans Epithelial Electric Resistance; IL-6: Interleukin 6; IL-1: Interleukin 1; SOCS : Suppressors of Cytokine Signaling; IGF1 : insulin-like growth factor 1 ; IGFALS : insulin like growth factor acid-labile substance)

DON causes impaired growth in animals via a rapid induction of expression of proinflammatory cytokines, followed by up-regulation of several suppressors of cytokine signaling (SOCS) (Surai et Dvorska, 2005), capable of impairing growth hormone (GH) signaling. Oral DON exposure perturbs GH axis by suppressing two clinically relevant growth-related proteins, IGFALS and IGF1 (Kenneth, 2009). It also impairs the barrier function of the intestine by reducing the expression of claudin proteins implicated in the regulation of tight junction proteins and decreases trans-epithelial electrical resistance, thus resulting in an increased risk of trans-epithelial passage of both bacteria and endotoxins into the body (Pinton et al., 2009).

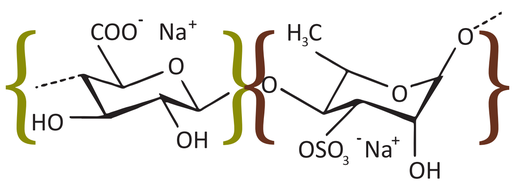
Endotoxins are derived from the cell membranes of Gram - bacteria. They are linked within the bacterial cell wall and are continuously liberated into the environment at cell death, during growth and division. Endotoxins act through activation of the immune system, with the release of a range of proinflammatory mediators, such as IL-6 and IL-1. This chain reaction leads to an increase of SOCS which have a negative action on GH-induced gene expression in liver, reducing the production of IGF1 and alleviate its many actions of growth hormone that have impact on productivity (growth, milk production, fertility…) (Kenneth, 2009). This synergistic effect between DON and endotoxins has been illustrated in different publications (Islam et al., 2005; Zhou et al., 2000; Döll et al., 2009).

Limiting the absorption of DON in the intestine by using interspaced clay closes the door to endotoxins and pathogens and reduces its combined and dangerous effects on the immune response and IGF1.

2.Interspaced clay, the tool to reduce DON absorption

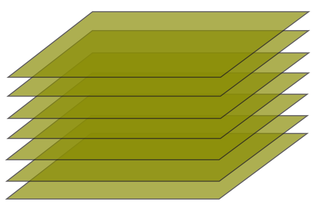
2.1 What is interspaced clay?

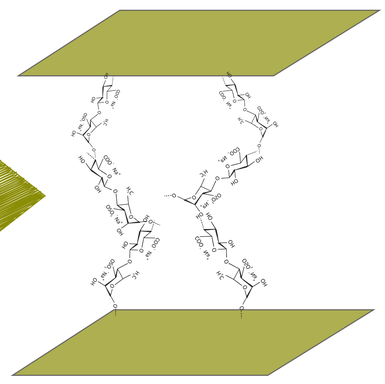
ULVANS
Ulvans are polyanionic polysaccharides, more specifically sulfated xylorhamnoglucoronans.
They are formed by a succession of disaccharides composed of an uronic acid (glucuronic acid or iduronic acid) and a sulfated rhamnose.



Uronic acid **Sulfated rhamnose**

MONTMORILLONITE
Clays within one same family can be very different from one to another. Montmorillonite clay belongs to the group of Smectites. It is a 2:1 Phyllosilicate, organized in a succession of layers, each one being composed of two Silicium sheets surrounding one Aluminium sheet. The interlayer space of montmorillonite type clays, varies from 0.25 to 0.7 nm (with water).





Increase of the interlayer space

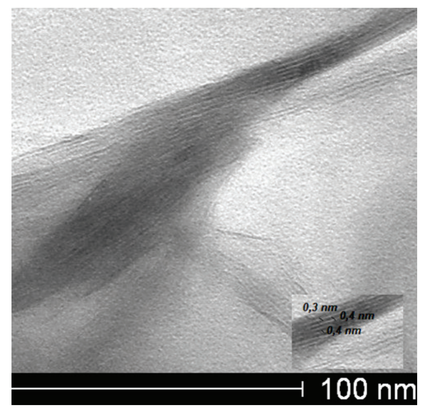


Chart 2: TEM picture of montmorillonite

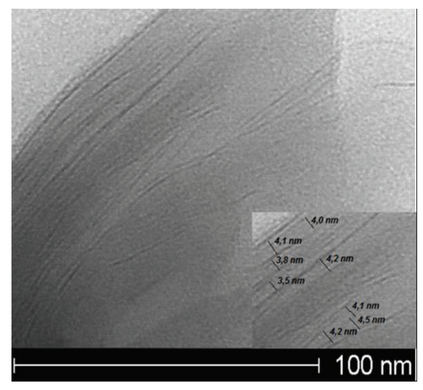


Chart 3: TEM picture of interspaced montmorillonite

2.2 Efficacy of interspaced clay on DON

The absorption of DON from the jejunum (jej) and ileum (il) compartments and from both compartments together (total) was measured after the addition of interspaced clay in the TIM-1 system of pig feed contaminated with 0,8ppm of DON (Chart 4).
The bioaccessibility of DON from contaminated pig feed was not significantly inhibited by the addition of interspaced clay at the level of 0.01%. However, a strong inhibition of absorption was found by the addition of interspaced clay at the level of 0.1%. The reduction was approximately 40% in comparison to the control (Havenaar et Demais, 2006).

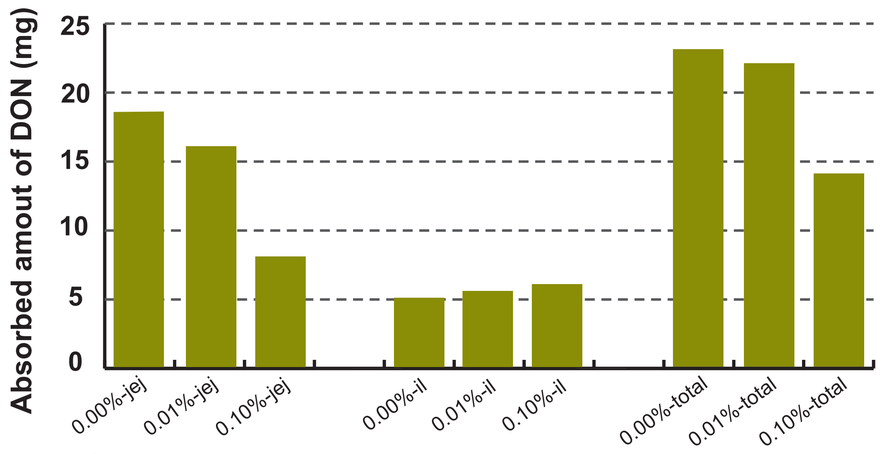


Chart 4: Reduction of DON absorption with interspaced clay

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