Deoxynivalenol in the intestine
What actually happens?

Christina Schwab  PhD
Product Manager, Mycotoxin Risk Management
Deoxynivalenol in the intestine
What actually happens?

Out of 12,947 scientific publications on mycotoxins, more than 3,000 deal with deoxynivalenol. Scientists have only begun to investigate the effects of deoxynivalenol on the intestine of animals in the last decade, and data is still very much limited.

Several *Fusarium* strains are capable of producing deoxynivalenol (DON, vomitoxin) a type-B trichothecene. The common active group of all trichothecenes is the epoxide, which is responsible for the binding of DON to ribosomes inhibiting protein syntheses. The non-toxic de-epoxidated metabolite DOM-1 cannot bind to ribosomes due to the lacking epoxide group.

It is important to know that DON can be further modified into several different metabolites by fungi, plants, animals, and bacteria (see Table 1). These DON derivatives are also called masked mycotoxins.

Studies have shown that the amount of DON derivatives, mainly 3/15AcDON and D3G, can account for an additional up to 75% of DON contamination in feed. Newly released wheat cultivars, which are able to more efficiently convert DON to D3G, are more resistant towards the DON producing fungus *Fusarium graminearum*, but can contain up to 10-times more D3G than DON.

What happens to DON and its derivatives when they enter the gastrointestinal tract (GIT) of an animal?

**DON after ingestion**

The intestinal absorption of DON and its metabolites differ between animals. The localisation of the gut microbiota before the small intestine has a major effect on bioavailability, as DON is mainly absorbed in the small intestine.

In swine, one of the animals most sensitive to DON, the microbial biomass in the stomach—which is located before the small intestine—is only in the range of $10^2$-$10^3$ per mL intestinal fluid (Figure 1). About 54–89% of DON can cross the intestinal epithelium and are detected in the blood.

Intestinal bacteria can transform the DON derivatives D3G, 3/15AcDON into DON. The transformation of DON into non-toxic DOM-1 by bacteria such as the active strain in Biomin® BBSH 797 prevents the absorption of DON.

In an experiment with 24 piglets, the concentration of DON in the blood serum was significantly reduced ($P<0.05$) when Biomin® BBSH 797 was added to DON-contaminated feed (Figure 2). DON is then eliminated as glucuronidated DON (D3GA, D15GA) via urine.

After ingestion of DON-contaminated feed, the intestinal epithelial cells are the first target of DON. Regardless of the amount of DON being absorbed, the intestinal epithelium is exposed to the entire contamination of the feed and therefore non-absorbed toxins can also compromise the entire intestine. Absorbed

---

**Table 1.** DON can be modified into several different metabolites by fungi, plant, animals, and bacteria, influencing its toxic effect.

<table>
<thead>
<tr>
<th>Metabolised by</th>
<th>DON-metabolites</th>
<th>Abbreviations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fungi</td>
<td>3-acetyl-DON</td>
<td>3AcDON</td>
</tr>
<tr>
<td></td>
<td>15-acetyl-DON</td>
<td>15AcDON</td>
</tr>
<tr>
<td>Plants</td>
<td>3-O-glucoside DON</td>
<td>D3G</td>
</tr>
<tr>
<td>Animals</td>
<td>DON-3-glucuronide</td>
<td>D3GA</td>
</tr>
<tr>
<td></td>
<td>DON-15-glucuronide</td>
<td>D15GA</td>
</tr>
<tr>
<td>Bacteria</td>
<td>De-epoxy-deoxynivalenol</td>
<td>DOM-1</td>
</tr>
</tbody>
</table>

---

**Figure 1.** Comparison of pH value and microbial density per mL intestinal fluid in swine.

- **pH gradient**
  - Stomach: 1.5-5
  - Duodenum: 5-7
  - Jejunum: 7-9
  - Ileum: 7-8
  - Colon: 5-7

- **Microbial biomass**
  - Stomach: $10^2-10^3$
  - Duodenum: $10^2-10^4$
  - Jejunum: $10^4-10^6$
  - Ileum: $10^9$
  - Colon: $10^{11}-10^{12}$

Source: Adapted from Maresca, 2013.
Regardless of the amount of DON being absorbed, the intestinal epithelium is exposed to the entire contamination of the feed and therefore, non-absorbed toxins can also compromise the entire intestine.

**Reduced intestinal barrier function**

The intestinal tract represents an important barrier to ingested chemicals, feed contaminants and the first line of defense against intestinal infection. The gut barrier is formed to a large extent by tight junctions that seal the luminal end of the intercellular space.

DON crosses the intestinal mucosa paracellular through the tight junctions. At the same time DON increases the paracellular permeability of the intestine through the opening of the tight junctions. Therefore, chronically exposed animals have a higher DON uptake.

More bacteria can also be translocated across the intestinal epithelium, increasing the risk of intestinal bacterial infections. Other mycotoxins, pharmaceuticals, pesticides, allergens, fungi and viruses are also granted an easier passage across the intestinal epithelium.

**Figure 2. Serum DON and DOM-1 concentrations in piglets**

Feeding piglets a diet contaminated with DON (1.8 mg/kg) or the same contaminated diet supplemented with the additive Biomin® BBSH 797 at a dose of 1.7 x 10^8 CFU/kg feed.

Blood was collected before feeding the contaminated diet (control) and 48h after the addition of DON +/- Biomin® BBSH 797.

Different letters (a,b for DON, A,B for DOM-1) above the columns within a given blood collection mean significant differences (P<0.05).

Source: BIOMIN

---

**Paracellular and transcellular route through the intestinal epithelium**

Paracelllar route
- If impairment:
  - Higher translocation of luminal antigens
  - Commensal flora
  - Pathogens
  - Food antigens
  - Toxins and mycotoxins

Transcellular route
- If impairment:
  - Lower uptake of nutrients such as glucose
  - Malabsorption of water

---

**What actually happens?**
mycotoxins can re-enter the intestine through the intestinal epithelium or through enterohepatic circulation (excretion via bile and re-absorption), thereby increasing the exposure time along the GIT.

**Poor intestinal function and nutrient uptake**

Seventy percent of the immune system is located in the GIT. DON harms the innate immunity by:

- direct activation of signal pathways
- opening of the tight junctions allowing luminal bacterial antigens to trespass
- reduced mucus production

High doses of DON repress the immune response whereas low concentrations promote a rapid mucosal inflammatory response, posing a risk of induced chronic intestinal inflammation, such as inflammatory bowel disease.

DON interferes with the intestinal absorption of nutrients, like glucose and amino acids. The sodium-glucose dependent transporter (SGLT-1) is responsible for glucose uptake. Low concentrations of DON are enough to inhibit SGLT-1 and therefore reduce glucose uptake. SGLT-1 is the most DON-sensitive transporter, followed by GLUT-5, the passive fructose transporter.

SGLT-1 is also responsible for water reabsorption and the blocking of SGLT-1 by DON could be the mechanism behind the oft-occurring DON-induced diarrhea.

Low doses of DON reduce the height of the intestinal villi, causing villus fusion and atrophy in the duodenum and jejunum of pigs. Villi increase the internal surface area of the intestinal wall and are therefore necessary for effective nutrient absorption.

**Feed refusal and anorexia**

Two well-known effects of DON are anorexia and feed refusal. The mechanisms behind these effects are complex and scientific evidence shows that within the gut-brain axis, neuroendocrine factors, pro-inflammatory cytokines and bitter taste receptors found throughout the GIT are involved in DON-induced feed refusal. The brain, particularly the hindbrain including the area postrema and hypothalamus, can signal immediate changes in food intake.

As DON is able to cross the blood-brain barrier, about 25–30% of the plasmatic DON can be found in the cerebro-spinal fluid of pigs after 2–60 min. On the other hand DOM-1 cannot cross the blood-brain barrier. A recent study also revealed that DON can alter brain functions and directly target the brain, causing vomiting, anorexia, fever, decreased locomotor activity and social withdrawal.

**References are available upon request.**