

# Finding the dietary solution to toxins, stress and immunity in dairy cows

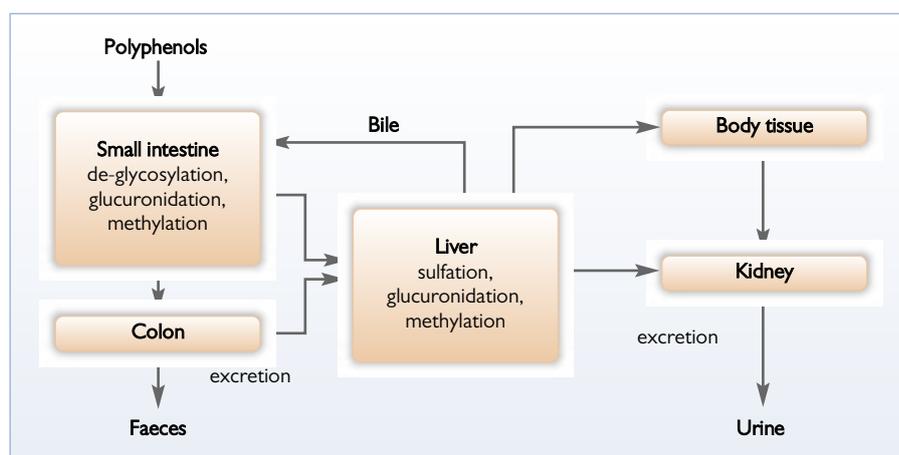
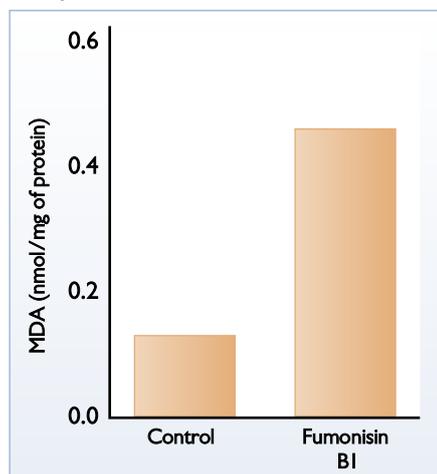
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The entire dairy industry, including consulting nutritionists, veterinarians and producers, all strive to keep their herd in good health knowing that healthy cows will be able to better cope with stress, especially with potentially contaminated feedstuffs.

Stress resulting in oxidative stress can negatively impact the dairy cow. Moulds and mycotoxins, endotoxins, hidden toxins in the feed, extra heat, pathogens challenges, environmental issues, changes in diets, transition period and calving all compromise the cow's immunity and its ability to deal with possible diseases, causing immune suppression. As a result, higher somatic cell counts, lower milk yield, poorer reproduction performance, mastitis and metritis, are observed.

Moulds are omnipresent. Their main task in nature is to decompose organic matter. More than 400 mycotoxins have been identified but about 20-30 are frequently detected with highly sensitive analytical methods (LC/MS-MS) in feed and food in higher concentrations. The most critical mycotoxins for ruminants are deoxynivalenol (DON), zearalenone formed by *Fusarium* spp. and aflatoxin B by *Aspergillus*.

**Fig. 1. Oxidative activity of fumonisin B1 on kidney cells (Abado-Becognee et al 1998).**



**Fig. 2. Metabolism of polyphenols.**

Fumonisin, ochratoxin A, ergot alkaloids as well as silage-associated roquefortin C and mycophenolic acid can also be detected.

The formation of mycotoxins undergoes significant regional and seasonal variation and among other things depends on the nutrient supply, water content in the substrate and in the surrounding air, temperature and pH. The optimum conditions for mould growth and toxin formation do not necessarily need to coincide.

Moulds and mycotoxins in feed cause chronic, 'subacute' problems in dairy cattle that show up with signs of higher disease incidence, reduced fertility or sub-optimal milk production. This is mediated by the following modes of action:

- Reduced intake or feed refusal.
- Altered microbial growth in the rumen.
- Reduced nutrient absorption and impaired metabolism.
- Altered endocrine and exocrine systems.
- Suppressed immune function.

Experience from research and practice indicate that individual actions are not sufficient. The best way to eliminate such risk related to the concurrent presence of toxic contaminants along with all other stresses inherent to the cows' production challenges seems to lay in a combination of actions – the cow metabolic support emphasising maintenance and balancing oxidative stress management, the essential organ (liver mainly) aid, the stimulation of rumen function and immune response, along with the

reduction of mycotoxins adsorption and toxins toxicity through their bio-transformation.

## Balancing oxidative stress

In biological organisms, such as the dairy cow, the antioxidant system and pro-oxidative substances (reactive oxygen species (ROS)) are finely regulated at the cellular level. Many studies have shown oxidative stress as a fundamental factor of unwanted immune and inflammatory responses.

Dairy cows, especially in the phase from gestation to lactation, are susceptible to a variety of diseases. ROS affect the regulation of gene expression, and the antimicrobial activity of the macrophages. Elevated levels of ROS damage nucleic acids, proteins and lipids, affecting important physiological functions.

Food spoilage and mycotoxins are considered oxidative stress triggers. It is not yet completely clear whether this is done by direct stimulation of the formation of ROS or indirectly by weakening the antioxidant system. Presumably, both paths are taken. In most cases, the levels of natural antioxidants are reduced due to lipid peroxidation caused by mycotoxins.

Fumonisin B1 was found to be a strong inducer of malondialdehyde (marker of oxidative stress, see Fig. 1).

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The antioxidant system of the mammalian cell is complex and consists of proteins, enzymes, vitamins and pro-vitamins, which are found in the cytosol, mitochondria or cell membrane. Special secondary plant metabolites such as the polyphenols can stabilise the existing system. Polyphenols are a complex group of substances, which can be divided into phenolic acids and flavonoids and being subdivided much further. They have an important role in building the cell walls that protect the plant from harmful influences such as UV light and pathogens and are involved in the repair of cellular damage.

The absorption of the polyphenols occurs mainly in the small intestine (Fig. 2). They may be chemically modified, bound on albumin to become water soluble and reaching the liver via the portal vein. In the liver, other molecular changes take place, such as hydroxylation, decarboxylation and conjugation, having the polyphenols become hydrophilic and excreted via the kidneys in the urine.

Thus, the main sites of action for polyphenols are the intestinal mucosa, liver, and kidney. The structural variability of polyphenols is also reflected in their effect. For example proanthocyanins are very poorly absorbed and their effect remains limited on the intestinal mucosal area.

Flavanones and isoflavones show the best bioavailability and can exert their antioxidant potential in blood, liver and kidney. However, the concentrations fall quickly after stopping supply, so that constant feeding is necessary. The antioxidant potential of polyphenols can be measured in relation to vitamin E in Trolox equivalent antioxidant capacity (TEAC), showing a broad variation of <0.1 to >5.0 mM TEAC per mM polyphenol. Therefore the usage of polyphenols presupposes their effectiveness in terms of absorption and antioxidant capacity.

## Supporting liver function

Crucial organs, like liver, are stressed and damaged or malfunctioning due to the presence of mycotoxins (aflatoxin and fumonisin) after absorption, while immune function is compromised by most of the other mentioned toxins.

The liver has a very high metabolic activity that makes it extra vulnerable for oxidative stress by aggressive molecules. In addition, the liver of dairy cows during early lactation is exposed to specific extra stresses. Low concentrations of glucose and insulin in the blood and increased influx of free fatty acids lead to fat deposition in the liver. Moulds and mycotoxins can exacerbate this further by reducing feed intake.

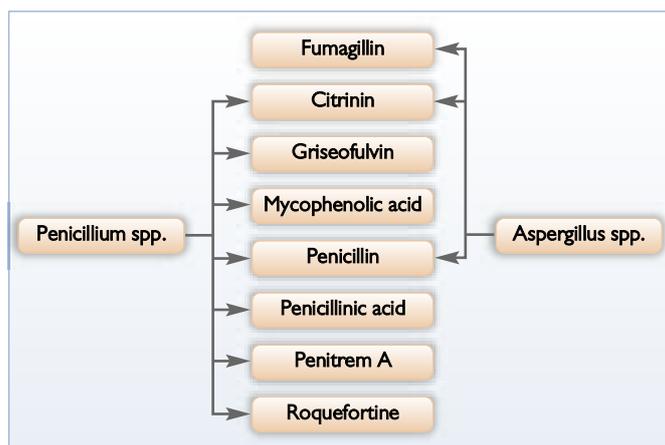


Fig. 3. Antibiotics produced by *Penicillium* and *Aspergillus* spp.

Some herbal ingredients have been proven to protect the liver. Experience with various parts of plants or extracts are supported by trials with cell cultures (in vitro model), animal studies (in vivo model) and clinical trials in humans.

Rosmary is well known for its strengthening effect on liver functions. Production and flow of bile are stimulated, so that the digestion is improved. The glucuronidation of unwanted molecules is increased, leading to accelerated elimination via urine and diminishing their potential disease impact. Artichoke leaves are a liver detoxifying and regenerating agent. It is mainly used to treat liver dyspepsia and disease. Main active components are cynarine and other bitter substances resulting in the regulation of lipid digestion.

## Stimulating rumen function

It should always be considered that mycotoxins will adversely impact rumen environment and activity even before having an effect on the animals themselves. Decreases in ruminal motility, on dry matter intake, acid detergent fibre (ADF), starch digestion and on microbial growth are some of the issues seen in animals fed mycotoxin contaminated diets, directly impacting production and indirectly initiating other metabolic disorders.

Additionally, toxins like aflatoxin and deoxynivalenol reduces feed intake and by consequence further suppression of nutrient supply. In dairy cattle, T2-toxin has been associated with intestinal haemorrhages, bloody faeces, gastrointestinal lesions and enteritis, finally disrupting the digestive process in the lower part of the digestive tract.

Moulds also produce antibiotics to defend themselves against other mould and bacteria. Fig. 3 shows some antibiotics produced by *penicillium* and *aspergillus* spp. present in silages. These antibiotic activities will suppress bacterial production in the rumen and lead to decreased feed conversion as well as 'normal' toxic effects of mycotoxins.

Fermentation extracts can maintain rumen

functioning and performance even in the presence of mycotoxins. They supply micro-nutrients like B vitamins, branched fatty acids and oligopeptides to a variety of bacteria and protozoa and stimulate their growth and efficiency acting therefore as prebiotics.

Cellulolytic bacteria are especially supported and may be increased in numbers by about 50%, bacteria +15%. As a result, the digestibility of organic matter, ADF and hemicellulose are improved. The production of short-chain fatty acids can be increased indicating higher energy supply from feed fibre.

## Supporting immune function

Mycotoxins appear to have a significant immunotoxic potential, depending on the degree of exposure. Gliotoxin produced by *A. flavus* acts as an immunosuppressive, being antibacterial and improving apoptosis. These effects can be enhanced further by T-2 toxin, as it inhibits phagocytosis of *A. fumigatus* conidia by macrophages. Direct effects of T-2 toxin are seen in lower concentrations of plasma immunoglobulin, and protein. Cows in phases of stress as in early lactation or due to high temperatures are particularly susceptible to mycotoxins because their immune system is already overtaxed.

The interactions between the immune system and nutritional status or requirements are well documented. The requirement of the immune system is highly dependent on the immune response and applied conditions. The system is less stressed when vital organs such as the liver are fully functional.

The rumen has great potential to eliminate toxins, if the microflora is well balanced and very active. In addition, the immune system can be activated directly.  $\beta$ -glucans, as extracted and concentrated yeast cell walls, can activate leukocytes and cytokines. Cytokines are peptides and some regulate growth and differentiation of cells, others are mediators of immunological reactions. The stabilisation of the immune system results in fewer cases of mastitis, and lower concentration of somatic cell count.

## Conclusion

At the beginning of lactation, during high mobilisation of body reserves and with high feed bypass through the rumen, the cow can barely cope with an additional burden like mycotoxin contamination. A multi-functional approach should be used to maintain and to stabilise the health of the cow naturally. Innovad's Escent can keep the liver and kidney healthy, as well as the rumen highly productive, resulting in more milk. ■