How exactly do mycotoxins work at molecular levels?

Professor Peter Surai explains

While more than 300 mycotoxins have been shown to induce signs of toxicity in mammalian and avian species, little is known about how they really work. Since mycotoxin chemical structures and properties are diverse, molecular mechanisms of their action include alterations in various metabolic processes in the body.

Three major mechanisms include:

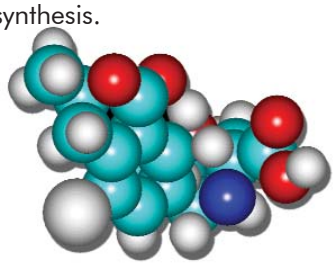
- Inhibition of protein, DNA and RNA synthesis and DNA adduct formation
- Membrane structure alteration and induction of lipid peroxidation
- Induction of programmed death of cells (Apoptosis)

1. INHIBITION OF PROTEIN, DNA AND RNA SYNTHESIS AND DNA ADDUCT FORMATION

It has been shown that molecular mechanisms of action of a number of mycotoxins involve their direct or indirect effects on major cellular events including protein, DNA and RNA synthesis.

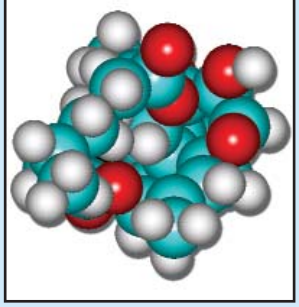
OCHRATOXIN A

Ochratoxin A (OTA) inhibits a specific enzyme involved in protein synthesis thereby substantially reducing an efficiency of protein synthesis. The alterations in protein synthesis could adversely affect DNA and RNA synthesis.



T-2 TOXIN

T-2 toxin is shown to inhibit protein, DNA and RNA synthesis in cells.

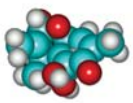


Immunosuppression, hepatotoxicity, nephrotoxicity, neurotoxicity, genotoxicity

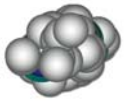
Increased mortality, poor feed conversion, poor growth rate, feed refusal, decreased fertility and hatchability

2. ALTERING MEMBRANE STRUCTURE

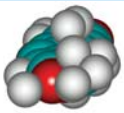
It is widely believed that mycotoxins can stimulate lipid peroxidation in target tissues. This was shown to occur as a result of action of OTA, T-2 toxin, aflatoxins, fumonisins, DON, zearalenone and other mycotoxins. This effect of mycotoxins in many cases is mediated by alteration in antioxidant defence. By changing concentrations of such antioxidants as vitamins E, C, carotenoids, glutathione as well as activities of antioxidant enzymes. Mycotoxins are able to induce peroxidation. Furthermore, as a result of their interactions with other prooxidants (Fe, Cu etc.) in biological systems and changes in redox status of the cell (a balance between antioxidants and prooxidants) occur.



DON



FUMONISIN



ZEARALENONE

Taking into account these mechanisms, our strategy to prevent mycotoxicoses includes various technological, chemical and other approaches to decrease mycotoxin levels found in the digestive tract. One of the most promising approaches we have found is to use an esterified glucan (Mycosorb*). Our results (*Surai and Dvorska, 2001*) showed that Mycosorb is able to prevent antioxidant depletion due to T-2 toxicoses in quails (Figure 1) and as a result to substantially decrease lipid peroxidation in the liver (Figure 2). Since lipid peroxidation is involved in all three major molecular mechanisms of mycotoxin action, this approach, especially, when you combine it with an antioxidant (organic selenium and vitamin E, etc.) it is very effective in commercial animal and poultry production.

Figure 1. T-2 toxin decreases antioxidant levels in the liver while esterified glucan tends to restore.

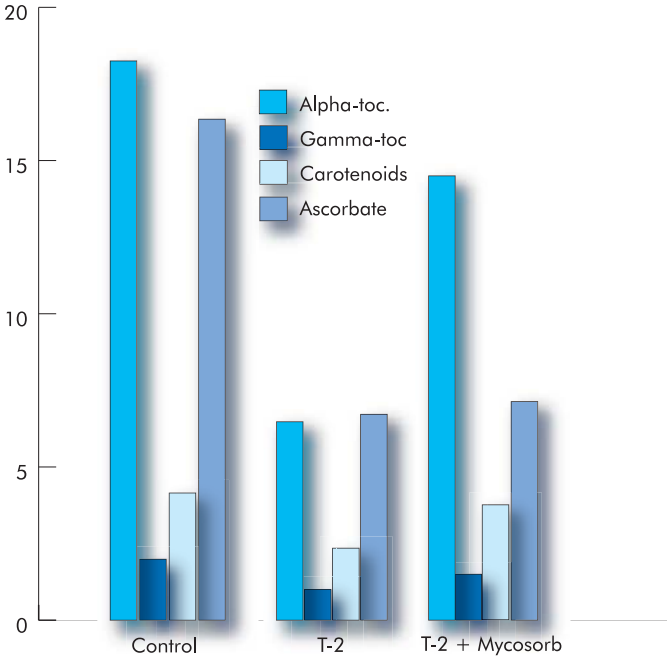
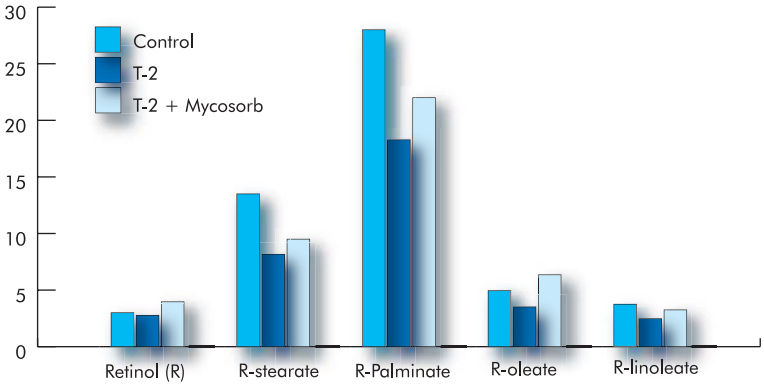


Figure 2. Effect of T-2 toxin and absorbents on vitamin A in quail.



3. INDUCTION OF PROGRAMMED DEATH OF CELLS

The maintenance of tissue homeostasis involves the removal of superfluous and damaged cells. This process is often referred to as 'programmed cell death' or 'apoptosis' since it is thought that cells activate an intrinsic death program contributing to their own demise. Apoptosis is characterised by cell shrinkage, nuclear pyknosis, chromatin condensation, DNA cleavage into fragments of regular sizes and activation of the cystein-proteases called caspases. It has been shown that T-2 toxin is a most potent apoptotic agent.

Mycotoxins can trigger apoptosis by directly affecting specific enzymes or via alteration of antioxidant/prooxidant balance in the cell, in particular by decreasing reduced glutathione concentration.