Mycotoxin interactions: An obstacle to risk assessment

In animal feed, multi-mycotoxin contamination is found quite frequently and seems to be the rule rather than the exception in practical diets. Here is a quick overview of the known interactions.

What are the most common mycotoxins in feed?

Mycotoxins represent an exceptional challenge for feed and animal producers: they are produced by common molds, occur in a great variety and number, are sporadic or heterogeneous in their distribution, and their effects on farm animals are seldom recognized as mycotoxicosis. Among hundreds of known mycotoxins, aflatoxins, mainly produced by Aspergillus species, ochratoxin A, produced by Aspergillus and Penicillium species, as well as fumonisins, trichothecenes (especially DON and T-2 toxin) and zearalenone, primarily produced by many Fusarium species stand out as the most common contaminants.

Consequences of mycotoxin contamination

Ingestion of these mycotoxins may cause an acute toxicity or chronic disorders, depending on the concentration and duration of exposure. In farm animals, this might manifest as decreased performance, feed refusal, poor feed conversion, reduced body weight gain, immune suppression, reproductive disorders, and residues in animal food products.

Due to their frequent occurrence and their severe toxic properties, many countries appointed legal regulations or guidance for the major mycotoxins to protect animals and human consumers. The current regulations are typically very specific in terms of animal species and even for the production stage considering that mycotoxins affect for example poultry in a different way than cattle and broilers in a different way than breeders or laying hens. The threshold and/or guidance values for each species, however, were determined based on toxicological data from studies investigating a monoexposure leaving out the possibility of any combined effects of mycotoxins.

Multi-contamination: the rule, not the exception

If we were able to ensure that the animals were exposed to only one mycotoxin at a time, following the regulatory guidelines would allow us to protect our animals in most of the cases. Several worldwide surveys show, however, that mycotoxin multicontamination of animal feed is found very frequently* and seems to be the rule rather than the exception in practical diets. The concurrent appearance of mycotoxins in feed can be explained as follows: each mold species has the capacity to produce a number of mycotoxins simultaneously. Each species, in turn, may infest several raw materials leaving behind one or more toxic residue. In the end, a complete diet is made up of various raw materials with individual mycotoxin loads resulting in a multitude of toxic challenges for the animals.

Several researchers showed that the effects observed during multiple mycotoxin exposure can differ greatly from the effects observed in animals exposed to a single mycotoxin, indicating that the simultaneous presence of mycotoxins may be more toxic than predicted from the mycotoxins alone. This is because mycotoxins interact with each other. The interactions can be classified into three main different categories: *antagonistic, additive,* and *synergistic.*

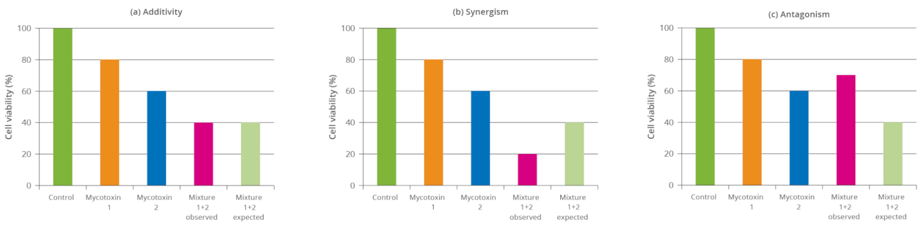
Types of mycotoxin interactions

Additivity occurs when the effect of the combination equals the expected sum of the individual effects of the two toxins (*Figure 1a*).
Synergistic interactions of two mycotoxins lead to a greater effect of the mycotoxin combination than would be expected from the sum of their individual effects (*Figure 1b*). A special form of synergy, sometimes called potentiation, occurs when one or both of the mycotoxins do not induce effects whereas the combination induces a significant effect.
When the effect of the mycotoxin combination is lower than expected from the sum of their individual effects, **antagonism** can be observed (*Figure 1c*). In general, most of the mycotoxin mixtures lead to additive or synergistic effects, highlighting a significant threat to animal health and being the major reason that impedes risk assessment. Synergistic actions may occur when the single mycotoxins of a mixture act at different stages of the same mechanism, e.g. T-2 increases ROS production while AFB1 decreases its clearance when the presence of one mycotoxin increases the absorption of another or decreases its metabolic degradation.

Be aware of contaminations

Given their complex interactions, the toxicity of combinations of mycotoxins cannot merely be predicted based upon their individual toxicities. Knowing that even low levels of mycotoxin combinations can harm animal productivity, health, and welfare, it is useful for feed and animal producers to be aware of present contaminations, to be able to link them to the risk they pose for the animal and consequently take actions before the problems appear in the field.

Figure 1 - Characterisation of the interaction between mycotoxins (Smith et al., 2016).



**References are available on request.*

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Using milk thistle to reduce liver damage from mycotoxins

Mycotoxins not only reduce animal performance, but they also cause significant liver damage.
The seeds of the herb plant milk thistle contain a mixture of flavonolignans known as silymarin and can help in reducing liver damage

when animals get in contact with mycotoxin contaminated feed.

Mycotoxins are a constant problem in cereals causing economic losses to the global animal industry. Mycotoxins are produced by filamentous fungi varying widely in their chemical and biological characteristics and effects on animals. Among the various mycotoxins, aflatoxins, and more specifically aflatoxin B1, is one of the most problematic because it affects maize, one of the major staple ingredients in animal diets worldwide. Of course, in nature, mycotoxins mostly occur in combinations, but even with singly contaminated ingredients, the nature of animal feeds leads to the concurrent presence of multiple mycotoxins, coming from the different ingredients. The separation of mycotoxins in polar and non-polar, however, simplifies their management. For example, aflatoxins (polar) are easily addressed by the inclusion of an adsorbent (like bentonite, for example). The same ingredient adsorbs not only aflatoxins, but also other mycotoxins, like zearalenone, ochratoxin A, and T-2 toxin, albeit at reduced efficiency.

Products limited to work in gut

Certainly, anti-mycotoxin agents are effective only while the feed is being digested, that is, while the feed remains in the lumen of the gastrointestinal tract. Anti-mycotoxin agents are not absorbed by the animal, whereas non-adsorbed mycotoxins are; leading to the need for further detoxification within the organism. Parts of mycotoxins might enter the organism despite the use of an anti-mycotoxin agent in feed due to the fact that no product is 100% effective, not all mycotoxins are affected similarly by a single product, non-polar mycotoxins might not be inactivated if only a polar agent is used, and vice versa and lastly, high contamination might render the normal dosage inadequate. This is often seen as being the most common cause, In other words, part of mycotoxins in the feed can still enter the animal. The exact effects on animal health and performance will depend, of course, on the initial contamination levels in the feed and on the constitution of the liver.

Mycotoxins and liver damage

Even short-term exposure to mycotoxins suffices to cause significant liver damage and loss of performance. In a study (Meissonnier, 2007), pigs were given 385, 867, or 1807 µg aflatoxin B1/kg feed for four weeks. Pigs receiving the highest level of aflatoxin developed clear signs of aflatoxicosis: hepatic dysfunction and decrease in weight gain. Also, the pigs exposed to the lower levels of mycotoxins showed clear signs of impaired metabolism and biotransformation. Additionally, mycotoxins and particularly aflatoxins inhibit the major hepatic biotransformation enzymes. This has significant consequences in veterinary medication applications as animals become unable to clear medications from their system – and of course, other toxins.

Read Using milk thistle to reduce liver damage from mycotoxins the full article

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