A global approach for the elimination of mycotoxins

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Are mycotoxins increasingly contaminating the food chain and thus threatening the survival of mankind? Although it may seem like it, that is not the case. It is true that hundreds of mycotoxins were detected during the last few decades. It is true that research each year elucidates extra effects which are caused by mycotoxins; invariably effects with a negative impact on performance, health or well being.

However, the basic message could be an optimistic one. Having been unaware of most mycotoxin effects until recently, the increased knowledge creates methods to better understand such effects and thus develop products that better eliminate mycotoxins.

A historical perspective

Mycotoxins were documented for the first time only some 50 years ago; in the aftermath of a huge outbreak of 'Turkey X disease', sufficient funding was spent on the detection of its cause: a huge contamination with aflatoxins.

Until the Turkey X disease outbreak, staple foods and feed were only investigated by UV light to diagnose an undefined level of aflatoxin contamination. Since then, analytical techniques drastically improved; this resulted in the detection of several hundreds of different compounds at continuously lower detection limits.

The evolution in detection limits from ppm or mg/kg to ppb or µg/kg also highly enlarged the number of effects that were found to be correlated with mycotoxins. Apart from clinical disease and death, more and more subclinical effects were highlighted.

Although one cannot predict how many mycotoxins still remain undetected, some authors estimate the total number at several thousands.

It is however mostly our knowledge about mycotoxins that is increasing, not the number of mycotoxins as such.

Mycotoxins must have been present in human nutrition before mankind started cultivating cereals. Historians already explain the '10th Plague of Egypt' as caused by trichothecenes in grain that was conserved too moist. The Greeks and the Romans had guidelines to store grains dried and aerated. Several medieval paintings show problems with 'Saint Anthony's Fire', which is nowadays known to be caused by Ergot mycotoxins.

As long as leaves have been falling from trees during autumn, fungi have been a driving force to convert those leaves into humus, thus fertilising soils. A number of fungi started growing on living plant material, while some of those must also have started producing mycotoxins. In other words: science does not invent new mycotoxins, but simply discovers long since existing ones and elucidates their effects.

So, the optimistic message is that further knowledge increase will lead to further improvement in animal performance, health and well being.

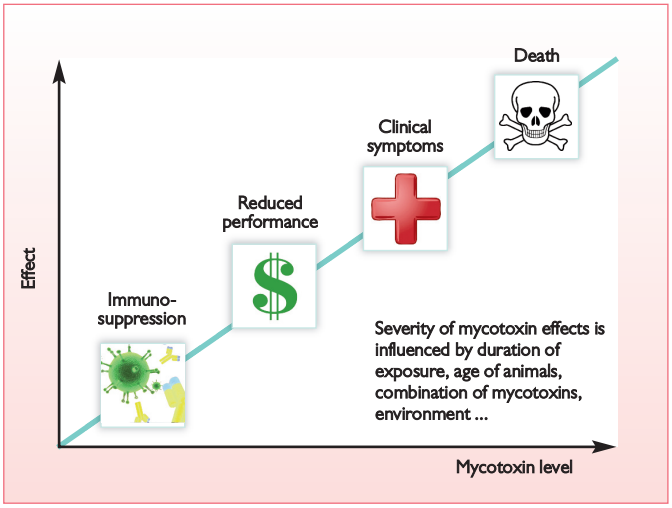

Fig. 1. Over the years, fine-tuning assay techniques allowed the elucidation of the impact of aflatoxins on a continuously expanding number of parameters: death at >5000ppb (1960s), liver impairment at >500ppb (1980s), poor DWG and FCR at >200ppb (1990s), reduced vaccination efficiency at >50ppb (2000s).

Combined mycotoxins

Only 20-25 years after attributing Turkey X disease to aflatoxins, the etiology was retrospectively updated as being a combination of aflatoxins with another mycotoxin: cyclopiazonic acid (CAP).

During the early sixties, only the ppm quantities of aflatoxins were detected, while the ppb quantities of CAP remained below the detection limit in those days.

By the mid-eighties, Aspergillus flavus was already known to often simultaneously produce AF+CAP combinations.

Because more than 100,000 turkeys died during the 1960 outbreak, the symptoms had been described in an elaborate manner; by 1986, it was obvious that not all symptoms were caused by aflatoxins, but that only a combination of AF+CAP provided a full explanation for all the symptoms.

Nowadays, combinations of mycotoxins are known to occur frequently. For certain combinations, the interactions have been studied; in most cases, the effects are additive (1+2=3), often synergistic (1+2>3), but only rarely antagonistic (1+2<3). So, combinations of mycotoxins generally are more harmful compared to contamination with a single mycotoxin.

Plants may try to detoxify mycotoxins, for example by conjugation or binding. Since such modified mycotoxins often escape detection during common assay procedures, they are called 'masked' mycotoxins. Plant geneticists try to amplify such characteristics to breed resistant crops, which might or might not be to the benefit of humans or animals consuming such crops.

The problem is that such masked mycotoxins are not always less toxic to humans or animals; even when

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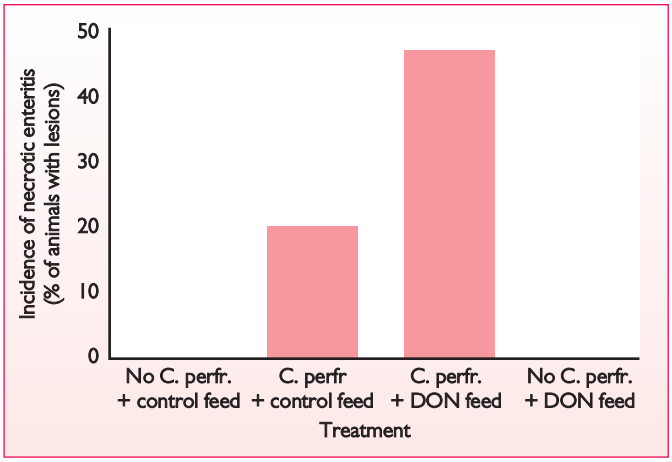
Fig. 2. The impact of DON on necrotic enteritis (Atonissen et al, 2014).



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being less toxic, the digestive tract may revert masked mycotoxins to their original, toxic form (for example by hydrolysis of the conjugation). So, the phenomenon of masked mycotoxins not only makes their analysis more challenging, but also the definition of maximum allowable limits.

For decades, ruminants were considered to be less susceptible for mycotoxins; the rumen microflora was considered to detoxify mycotoxins. The effect of the rumen is however highly variable.

With certain mycotoxins, rumen transformation even leads to intensification of the toxic effect: for example the metabolite zeranol is readily absorbed, while being more toxic than the original zearalenone. Vice versa, other mycotoxins are toxic for (part of) the rumen microflora: for example patulin.

Metabolites may also behave differently, while remaining toxic: for example aflatoxin M1 is more readily secreted with milk compared to the original aflatoxin B1.

Metabolisation of mycotoxins complicates research, since a multitude of compounds has to be assayed and tracked nowadays; from one single mycotoxin, as much as 5-10 different metabolites may be formed. Broad research is however beneficial, since it enlarges our understanding of the mechanisms involved; many metabolites serve as 'biomarkers' that help differentiate for example elimination from toxic reactions, long term from short term effects, etc. So, as long as funding is adequate, broad based research gives extra progress.

Mycotoxins and gut health

A malabsorption syndrome is a common result of exposure to aflatoxins, ochratoxins or trichothecenes. This worsens performance as measured by DWG and FCR. Apart from reduced absorption of proteins and other soluble nutrients, reduced tissue levels of vitamins with antioxidative properties, such as vitamin E, are also problematic; this has an impact on meat quality and reduces resistance against systemic infections (and cancer in humans).

Ochratoxin A was shown to increase both the incidence and the severity of salmonella infections in both broiler chickens and layers. Similar effects were noticed with coccidiosis as recorded by lesion score and oocyst index.

Mycotoxins may well be triggering factors reverting latent or controlled infections into clinical diseases.

Gut health is a motive to further reduce mycotoxin levels. The long established EU guidance value for DON in poultry is 5.0ppm in contrast to 0.9ppm in pigs; since the crop microflora was assumed to detoxify DON, the guidance level was higher for poultry compared to pigs.

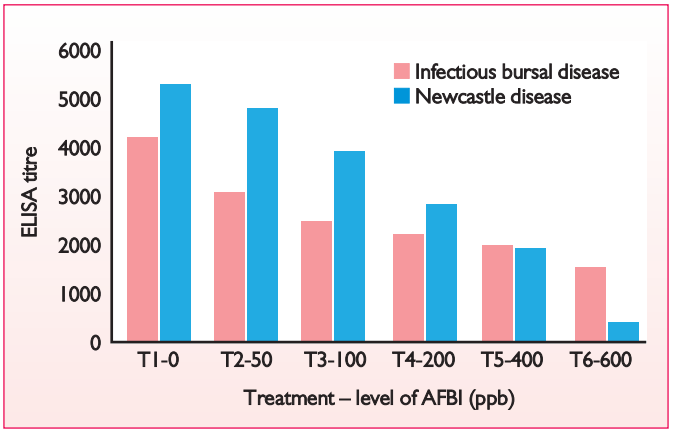

Fig. 3. The effect of graded levels of AFB1 on titres after vaccination (Manegar et al, 2010).

However, in a recent study it was highlighted that DON predisposes for necrotic enteritis in poultry at levels already well below the guidance level.

DON decreased nutrient absorption, increased barrier permeability and leakage of plasma AAs into the gut, which all contributed to proliferation of C. perfringens resulting in necrotic enteritis. The authors therefore plead for a reduction of the EU guidance level for DON in poultry.

Mycotoxins and immunity

Different mycotoxins have a different impact on the immune system. Aflatoxins are known to reduce the innate immunity (by inhibition of phagocytosis by macrophages) as well as the acquired immunity (by decreasing the number of T-lymphocytes, complement activity and cytokine production).

Ochratoxin A primarily affects antibody-producing cells, thus decreasing immunoglobulin synthesis. Also with DON and fumonisins diverse effects were highlighted. From an economical viewpoint, a well balanced immune system is important. Poultry farms traditionally invest a lot in vaccination.

However, it is common knowledge that the accuracy of such vaccinations may fluctuate, even though complying with all practical precautions. Trials confirm that mycotoxin contamination may jeopardise such efforts. Already at moderate contamination levels, aflatoxin B1 may significantly reduce the ELISA titres obtained after IBD or ND vaccination.

The impact of mycotoxins on vaccination can be highly insidious: even in ovo contamination with AFB1 impairs the after hatch vaccination of the birds. An efficient anti-mycotoxin program will also improve the reliability of vaccination programs.

Mycotoxin elimination

Mycotoxin surveys invariably show that a high percentage of feedstuffs are contaminated with mycotoxins. The more mycotoxins assayed, the higher the percentage of combined contaminations; by increasing the number of mycotoxins tested from only the traditional ones to a 37+ program, one may conclude that the average number of mycotoxins per sample is as high as 7.99, but what would be the outcome if as much as 370 mycotoxins were assayed?

There is discussion about the guidelines that define allowable limits for part of the mycotoxins. Partly due to economic considerations – a zero risk policy may put the food supply at stake – the concerned guidelines largely remained unchanged, even though research continues to reveal negative effects at always lower contamination levels.

Apart from a direct effect on performance, also indirect effects on gut health, vaccination efficiency, etc. compensate for an investment in a mycotoxin elimination program.

Prevention must be the first step, since it has a very pronounced effect on mycotoxin levels. Amongst other precautions, the use of products that inhibit mould growth (for example Moldstop), will reduce post-harvest contamination.

Further elimination of the mycotoxin impact however requires a pragmatic approach. In practice, it is not feasible to adequately assay the level of each mycotoxin in each feedstuff at each delivery.

Impextraco has therefore adopted a more global approach. In order to eliminate the mycotoxin effects to the best possible extent, a product should:

- Bind mycotoxins, so that they are eliminated with the faeces.
- Enzymatically detoxify mycotoxins in order to render them harmless.
- Protect gut integrity, thus reducing mycotoxin absorption from the gut.
- Stabilise immunity.
- Maintain liver health as this is the body's primary organ for detoxification.

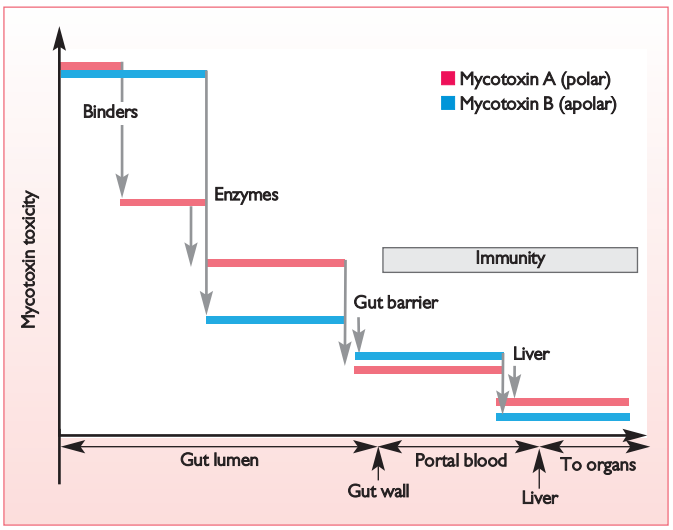

Fig. 4. Elitox combines several options for mycotoxin elimination.

Conclusion

Recent research detects an increasing number of different mycotoxins and produces evidence for their negative impact at lower and lower contamination levels.

Apart from direct effects on performance (DWG and FCR), their economic importance via indirect effects (gut health, immunity) is increasingly obvious. Even ruminants are not spared, while guidelines for monogastric animals appear too tolerant.

The complexity requires a pragmatic and global approach: apart from direct mycotoxin elimination, the animal's defence mechanisms should also be optimised. Elitox has proven on a global, worldwide scale to do that. ■

References are available on request from the author