



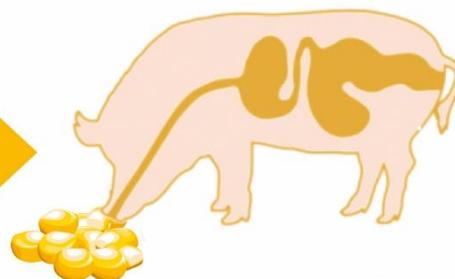
MyToolBox

THE SMART WAY TO TACKLE MYCOTOXINS

©Copyright: BIOMIN GmbH, 2017



Mycotoxin contaminated feed



Gastrointestinal detoxification

FEED ADDITIVES FOR MYCOTOXIN DETOXIFICATION

EFFICACY & AUTHORISATION

This article provides an overview of the different types of additives intended for use in animal feed for mycotoxin detoxification, and explains how the EU requires risk assessment by EFSA to demonstrate safety and efficacy.

FEED ADDITIVES FOR MYCOTOXIN DETOXIFICATION

EFFICACY & AUTHORISATION

INTRODUCTION

Feed additives for mycotoxin detoxification are substances which, when incorporated into animal feed, either bind mycotoxins so they are no longer bioavailable or they act as bio-transforming agents converting the toxins into less toxic products. There is a vast scientific literature covering mycotoxin detoxification in animal feed and a large number of substances have been advocated as physical or biological adsorbents or microbiological/enzymatic transformation agents. Recent reviews have covered mycotoxin detoxification by adsorption or transformation [1] providing an overview of types of feed detoxifying agents and their reported efficacy in both *in vitro* and *in vivo* systems [2]. Particularly exhaustive is a 2009 report commissioned by EFSA to review mycotoxin-detoxifying agents used as feed additives, their mode of action, efficacy and feed/food safety [3].

The schematic below [adapted from 2] provides a good overview of the wide range of adsorbing and bio-transforming agents which have been proposed as detoxification additives for use in animal feed. However, the reality is that whilst, particularly with *in vitro* systems, it is possible to demonstrate the potential of a detoxification additive, moving from 'proof of principle' to an authorised and cost-effective commercially viable product is a huge scientific and financial challenge.

MyToolBox

An EU-funded project known as MyToolBox

www.mytoolbox.eu aims to publicise more widely the EU approach to approval of feed additives and in particular disseminate the guidance on demonstrating efficacy through *in vitro* and *in vivo* animal studies.

A particular focus of the project is to establish suitable collaboration on mycotoxin detoxification additives with partners in China.



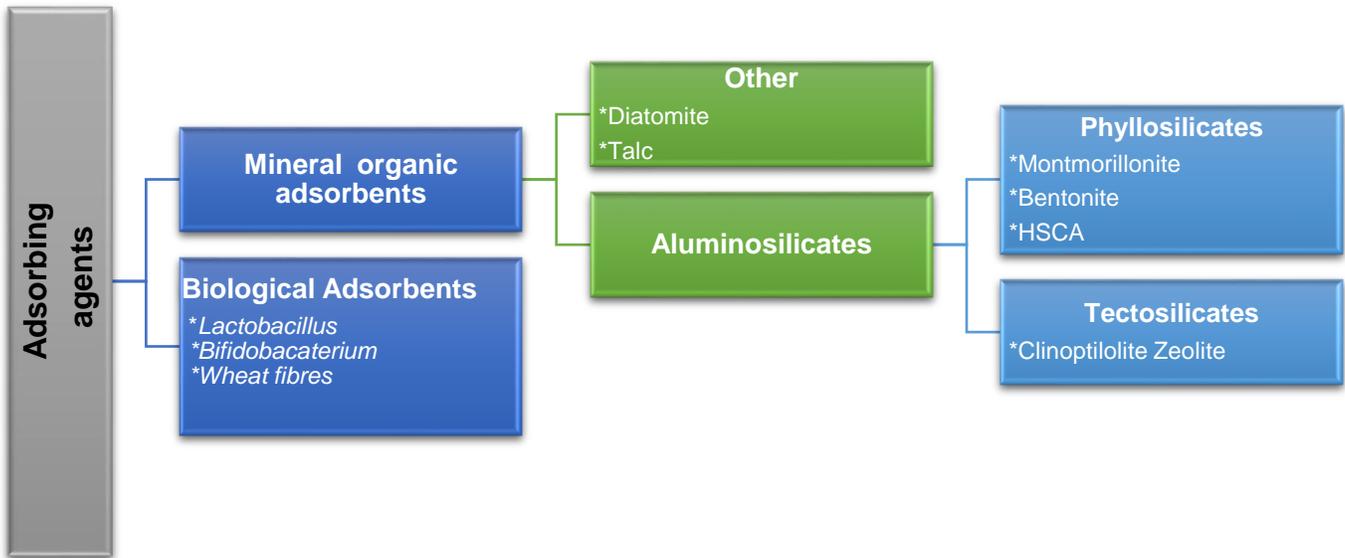


Fig 1a:- Classification of types of mycotoxin detoxification additives based on adsorption

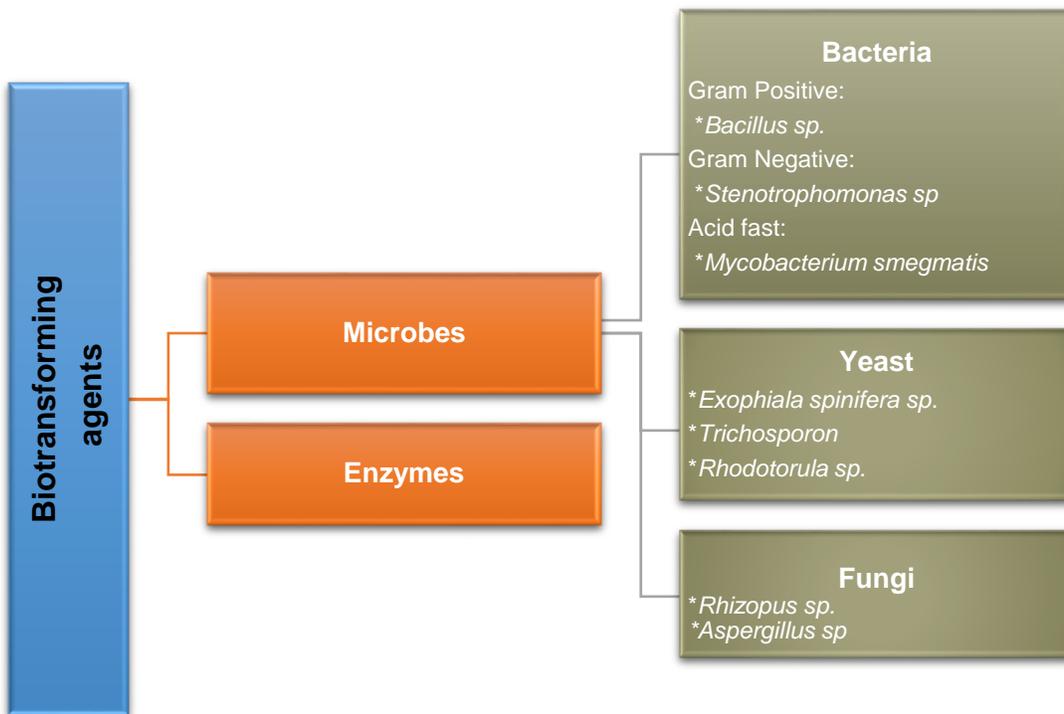


Figure 1b- Classification of types of mycotoxin detoxification additives using biotransformation

EU Regulations covering feed additives

Council Regulation (EC) No 1831/2003 sets out rules for the authorisation, supervision and labelling of feed additives. In the EU only additives that have been through an authorisation procedure may be placed on the market. Authorisations are granted for specific animal species, specific conditions of use and for 10 years after which time a re-submission is necessary. Within the category of technological additives, a new functional group of additives was created in 2009 described as 'substances for reduction of the contamination of feed by mycotoxins'. EFSA is responsible for conducting the evaluation of the data submitted requesting authorisations, and subsequent to a favourable EFSA opinion on the safety and efficacy of the additive, the European Commission can grant the final authorisation of the product.

EFSA risk assessment of feed additives for reduction of mycotoxin contamination

Feed additive producers requesting EU authorisation have to submit a dossier to the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP). There is specific EFSA guidance regarding design and content of dossiers for the purpose of binder/deactivators assessment. The dossiers are assessed by the FEEDAP Panel and the assessment is published on-line as an EFSA Scientific Opinion. Confidential data contained in dossiers is not made publically available.



The EFSA guidance requires petitioners specifically to provide information concerning:-

Properties of additive

Mode of action

Targeted mycotoxin(s)

Stability of additive

Evaluation of possible interference with nutrients/additives.

Assessment of combined effects of the additive and resulting metabolites on the safety of both animals and consumers.

Efficacy demonstrated by a minimum of three *in vivo* studies conducted in at least two different locations, employing preferably naturally contaminated feed with mycotoxin levels below the EC guidelines.

Results have to demonstrate product's safety as well as a significant improvement in the most relevant end-points such as excretion of toxin and/or metabolites, toxin/metabolite levels in blood and tissues, levels of biomarkers of exposure or the presence in products destined for human consumption such as eggs or milk. With respect to these studies the concentration of the mycotoxin used in the feed is particularly important. EFSA specifically states that 'The mycotoxin content in feed used in studies should not exceed the values given in Directive 2002/32/EC for aflatoxin B₁ and in Commission Recommendation 2006/576/EC for deoxynivalenol, zearalenone, ochratoxin A and fumonisins B₁+B₂ for complete feeding stuffs for the respective animal species/category. For mycotoxins without a maximum content established at EU level (e.g., T-2 and HT-2 toxins), the dietary levels chosen should not exert adverse effects in the target animals'. Zootechnical parameters, such as feed efficiency or weight gain should be reported, but by themselves do not constitute a measure of the detoxifiers efficacy.

EU approved feed additives for reduction of mycotoxin contamination

Once feed additives have been considered by EFSA if they receive favourable opinions there is then subsequent authorisation by the European Commission for use as substances for reduction of the contamination of feed by mycotoxins.

Bentonite

- It was authorised by the European Commission for use as an aflatoxin B₁ sequestering agent in ruminants, poultry and pigs.
- This was based on a number of published *in vitro* studies and an *in vivo* study in cows showing a reduction of aflatoxin M₁ transfer to milk by 40%.

BioMin® BBSH

- It is a bio-transforming product to be used in pigs, authorised in 2013 after demonstrating *in vivo* studies proving significant (about 70%) decrease of DON concentration in pigs' serum after contaminated feed ingestion, due to its bio-transformation into the less toxic, de-epoxy-DON. It obtained a positive EFSA opinion in Dec 2016 as a technological feed additive for all avian species and authorisation was granted in June 2017.

FUMzyme®

- It is a fumonisin esterase, which was authorised for pigs in 2014. Short and long-term feeding studies measured the ratio of sphinganine/sphingosine as a sensitive endpoint for fumonisin toxicosis, and found the ratio was significantly reduced in piglets by the addition of FUMzyme® at the minimum proposed dose.
- Similar finding for chickens and turkeys were published in a favourable 2016 EFSA Opinion and the authorisation was granted in May 2017.

Management of mycotoxin contamination in food and feed in China

A recent review provides some insights into the current safety management system for combating mycotoxin contamination of food and feed in China [4]. The importance of systematically managing risk assessments to ensure food safety has been accepted by the Chinese government. A risk assessment system and an expert committee for food safety were stipulated by the 2009 food safety law and the Administration Regulation of Food Safety Risk Assessment was announced, which prompted the formation of a new risk assessment organisation in 2011, known as the China National Centre for Food Safety Risk Assessment. This is the first specialised institute to systematically implement and manage risk assessment in China independent of government.

The tasks of the Centre include not only routine risk assessments, such as assessment of exposure to mycotoxins, but also the drafting of food safety standards and technical management protocols. With respect to risk assessment of feed, an expert committee was established to provide guidance related to the risk assessment of quality and safety of agricultural products. The Ministry of Agriculture (MOA) is currently speeding up the formulation of the Administration Regulation for Risk Assessment of Quality and Safety of Agricultural Products. The Chinese Academy of Agricultural Sciences (CAAS) has planned to establish a national research centre for risk assessment of quality and safety of agricultural products, comprising approximately 15 ministerial-level research centres and approximately 20 college-level research centres, to support risk assessment of feed and other agricultural products. The expert committees have been working closely together to ensure the development of comprehensive and efficient risk assessment protocols for food and feed.

As there is no international consensus on evaluating the efficiency of mycotoxin detoxifiers, at the present time there is currently no regulation on use of mycotoxin detoxifiers as a feed additives in China. As such, no standard protocol is available to verify the efficacy and safety of mycotoxin detoxifiers on the Chinese market. Nevertheless, there are mycotoxin detoxifying products available commercially in China which are listed in the raw materials catalogue (such as clay, hydrated sodium calcium aluminosilicate (HSCAS), montmorillonites, yeast cell wall, and some probiotics) promulgated by the MOA.

Notwithstanding the lack of a regulatory framework for feed additives, it is notable that an 'Aflatoxin-Detoxifzyme' additive was approved by MOA in 2010 as a new feed additive/enzyme. In recent years the MOA has attached great importance to controlling mycotoxins in animal feed. In 2013, the Feed Research Institute of CAAS was commissioned by the MOA, to initiate a 5-year project, entitled "Mycotoxin Detoxifying Feed Additives Evaluation Standard Researching". The project is carrying out a survey of mycotoxin detoxifiers in the market of China, comparing methodologies and evaluating the efficiency of the mycotoxin detoxifying feed additives both *in vitro* and *in vivo*. The results of the project will report to MOA, as a basis of setting up future standards for mycotoxin detoxifying feed additives.

MyToolBox initiative on feed additives for mycotoxin detoxification



MyToolBox is an EU project funded through the Horizon 2020 research programme. The wide ranging project with 23 partners from 11 countries started in March 2016 and will be completed in 2020. More details concerning the project can be found on the dedicated website www.mytoolbox.eu. The project aims to develop novel measures to minimise fungal infection and mycotoxin formation and to provide advice to farmers and others in the food and feed chain. The project also addresses measures to minimise the impact of mycotoxins in animal feed and proposes to conduct two animal feeding studies in China. These studies will compare the efficacy of EU-authorised aflatoxin and fumonisin detoxification feed additives with comparable additives produced in China. The studies will be conducted using cows and pigs for aflatoxin and fumonisin respectively and will follow guidance set out by EFSA for evaluation of dossiers. The aim is to establish collaboration in

China on risk evaluation of feed additives, as well as facilitating dialogue and a knowledge transfer in terms of these very specific *in vitro* animal studies. The particular expertise relates to animal feed study design with appropriate controls, as well as undertaking appropriate biomarker measurements.

MyToolBox uniquely has partners with mycotoxin and specifically feed additive expertise from Government, FEFANA, academia and from commercial companies in this area. MyToolBox facilitated a 'round-table' meeting of experts in Beijing in March 2017 which included an official from the European Commission and officials from the MOA and CAAS-FRI. This round-table discussed how the different approaches in the EU and China for handling mycotoxin detoxification feed additives studies can be used for standard setting. The importance of the ongoing MyToolBox animal feeding studies were also acknowledged.

References

- [1] Jard et al., (2011) Review of mycotoxin reduction in food and feed: from prevention in the field to detoxification by adsorption or transformation, *Food Additives & Contaminants: Part A*, 28:1590-1609,
- [2] Wielogórska et al., (2016). A review of the efficacy of mycotoxin detoxifying agents used in feed in light of changing global environment and legislation. *World Mycotoxin Journal*, 9: 419-433
- [3] EFSA (2009) Review of mycotoxin-detoxifying agents used as feed additives: mode of action, efficacy and feed/food safety. EFSA Scientific Report FEEDAP 2009-01
- [4] Zhang et al., (2014) Management of mycotoxin contamination in food and feed in China. *World Mycotoxin Journal*, 7: 53-62

