ANNALS OF ANIMAL SCIENCE
ISSN: 2300-8733, https://sciendo.com/journal/AOAS

ACCEPTED AUTHOR VERSION OF THE MANUSCRIPT:

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DOI: 10.2478/aoas-2023-0087

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Received date: 9 December 2022

Accepted date: 18 September 2023

To cite this article: (2023). Bočarov-Stančić A., Lopičić Z., Krstović S., Krulj J., Milojković J., Maslovarić M., Bodroža-Solarov M. (2023). Agents of different origins for reduction of mycotoxins' level in feed, Annals of Animal Science, DOI: 10.2478/aoas-2023-0087

Agents of different origins for reduction of mycotoxins' level in feed

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Abstract

Toxic secondary metabolites of some fungi (mainly representatives of *Alternaria*, *Aspergillus*, *Fusarium* and *Penicillium* genera) may contaminate agricultural products, representing serious health hazards both to humans and animals. Along with this, the economic losses due to the mycotoxins' presence in feed production, including crop and animal feedstuff processing and distribution, motivated the plentiful research of detoxification strategies. Feed supplementation with mineral adsorbents (zeolites, hydrated sodium calcium aluminosilicate (HSCAS), bentonites, etc.) is the most prominent approach widely applied. Besides these, other products for mycotoxin level reduction based on the constituents of the yeast cell wall or *Lactobacilli* are often used. Recently, many investigations are directed toward plant-derived products that can efficiently adsorb mycotoxins in their native (biosorbents) or modified forms (e.g. activated carbon, biochar etc.). These renewable, easily accessible and readily prepared sorbents are economically viable and safe alternatives for mycotoxin decontamination of feed resources. Organic polymers (chitosan, cellulose, etc.) as well as synthetic polymers, such as polyvinyl pyrrolidine, also might reduce mycotoxins' level in feed. Besides these conventional methods, new research trends are nanotechnologies, the promising, effective, low-cost way for mycotoxins' removal. This overview systematically summarizes information on binding agents of different origins for the reduction of mycotoxins' levels in feed. Furthermore, the knowledge of potential applications of binding agents in the feed industry is also reviewed and discussed.

Key words: mycotoxins reduction, feed, mineral adsorbents, plant-derived products, polymers, nanoparticles

The Codex Alimentarius is a collection of standards, guidelines and codes of practice adopted by the Codex Alimentarius Commission (CAC), which is the central part of the Joint FAO/WHO Food Standards Programme. It incorporates advice on food/feed management methods that can reduce the risk of contamination of food/feed with fungal secondary metabolites-mycotoxins, which cannot be removed completely. According to the research conducted in different parts of the world, on about 2000 samples from 52 countries, Kovalsky et al. (2016) reported that mycotoxin contamination in feeds could be up to 79% or higher. Also, a ten-year large-scale global survey of mycotoxin contamination in feed, that covered more than 70.000 samples from 100 countries, showed that 88% of the samples were contaminated with at least one mycotoxin, while 64% of samples was co-contaminated with ≥2 mycotoxins (Gruber-Dorninger et al., 2019).

Due to their frequent occurrence and toxicity, aflatoxins (AFs), zearalenone (ZEN), trichothecenes (deoxynivalenol-DON and T-2 add HT-2 toxins), ochratoxin A (OTA), and fumonisins (FUMs) are mycotoxins that can significantly impact the health and productivity of livestock. Because of that, many countries all over the world restrict these mycotoxins levels in food and feed by different regulations (Zain, 2011). The most important fungal genera responsible for contamination with mentioned mycotoxins are *Aspergillus* (*A. flavus* and *A. parasiticus* – AFs; *A. alliateus, A. ochraceus* and *A. niger* - OTA), *Fusarium* (*F. culmorum* and *F. graminearum*- DON and ZEN; *F. sporotrichioides* and *F. tricinctum* – T-2 and HT-2 toxins, *F. verticillioides* - FUMs) and *Penicillium* (OTA etc.) (Bräse et al., 2013). The biological activities of mycotoxins may be strong mutagenic and carcinogenic (AFs), nephrotoxic (OTA), hepatotoxic (AFs and FUMs) and immunotoxic (AFs, trichothecenes, FUMs) (Naehrer, 2014). Also, trichothecenes can adversely affect animals' food consumption, growth, reproduction, neuroendocrine signalling, and intestinal function (Pestka, 2010; Pinton et al., 2010). Accordingly, both humans and animals may be affected by mycotoxins, which can cause carcinogenic, mutagenic, teratogenic, immunosuppressive and endocrine-disrupting effects (Milićević et al., 2010). Factors such as temperature and water availability affect the life cycle of mycotoxigenic fungi. Their occurrence remains a global threat and with changing climate conditions, changes in mycotoxins patterns are anticipated. Therefore, in the future, the increased impact of mycotoxins entering the food supply chain can be expected (Magnoli et al., 2019).

Mycotoxins are a group of compounds with different physical and chemical characteristics that can be classified mainly as polar and nonpolar molecules, depending on their electrical charges. Highly polar (water-soluble) mycotoxins are AFs and FUMs, B type trichothecenes (e.g. DON) are polar, while ZEN, OTA and T-2 toxin are nonpolar (fat-soluble) molecules (IARC, 2012; Stroka and Maragos, 2016). Mycotoxins might coexist with other toxic and non-toxic compounds, also present in food and feed, interfering with the toxicity of mycotoxins. These conjugates, favoured by heat, can be found in the finished products, either in soluble form or incorporated into macromolecules (Di Gregorio et al., 2014).

Having in mind the presence of mycotoxins in food and feed and the numerous hazardous effects of mycotoxins on living beings, it is necessary to develop methods and strategies to eliminate mycotoxins' impact. According to Bata and Lásztity (1999) the following strategies can be used to reduce mycotoxin influence as a health hazard: prevention of

contamination, prevention of the mycotoxins' absorption by the digestive tract of the consumer or detoxification of food and feed contaminated with mycotoxins.

For human food and animal feed detoxification, a variety of chemical, physical or biological methods can be applied. Among the others, adsorption of mycotoxins by binding agents has significant importance, because of its high efficiency, low cost, non-destructive action on nutritional compounds in food/feed, low labour demand, etc. In this paper, information on binding agents of different origins for the reduction of mycotoxins' content in the feed is presented and discussed. The binding mechanisms resulting from different structures of binding agents are also reviewed.

Binding agents for mycotoxins

Besides of the preventive strategies, approaches have been employed including physical, chemical and biological treatments to detoxify AF in contaminated feeds and feedstuffs (Oguz et al., 2018). The most frequently used technique for reducing exposure to mycotoxins is to decrease their bioavailability by the inclusion of various non-nutritive and inert mycotoxin-binding agents or adsorbents. These agents form a complex with mycotoxins, thus prevent or reduce mycotoxins passage from the gastrointestinal tract into the blood and organs of animals (Liu et al., 2022). The efficiency of binding depends on the physical and chemical characteristics of the adsorbent as well as of the mycotoxin type. Features of a broad-spectrum mycotoxin adsorbent should be high adsorption capacity against either range of mycotoxins, safety, low non-specific binding to nutrients, affordability, stability and ease of incorporation into feed (Kabak et al., 2006; Pearce et al., 2010).

Complete mycotoxin control may require a combination of different approaches with varying modes of action because the adsorbents might have different mechanisms in protecting livestock against the detrimental effects of mycotoxins. Mycotoxins can be bound to adsorbents using different types of interactions such as hydrophobic bonding, hydrogen bonding, electrostatic interactions, and coordination bonds; the source of the toxins can also be eliminated by increasing the cell membrane permeability of the fungi (Pearce et al., 2010).

An important criterion for the evaluation of mycotoxin adsorbents is their effectiveness at different pH levels (acidic and neutral) (Bočarov-Stančić et al., 2011). The adsorbent must be efficient enough throughout the entire gastrointestinal tract and the mycotoxin–adsorbent complex should remain stable to prevent desorption of the toxin during digestion (Jard et al., 2011).

Mineral adsorbents of mycotoxins

Mineral adsorbents of mycotoxins, also known as clay minerals or inorganic binders, are considered to be materials of the "greening 21st century material worlds" (Ray and Bousmina, 2005). They are naturally abundant, non-toxic and low-cost, characterized by good adsorption performance, high chemical stability and biocompatibility (Li et al., 2018; Vila-Donat et al., 2018). The largest and most important class of clay minerals are aluminosilicates, which are composed of silica, alumina, and significant amounts of alkaline and alkaline earth ions (Moreno-Maroto and Alonso-Azcárate, 2018). Two of the most prevalent types of aluminosilicates are phyllosilicates, with extended layered structures, and tectosilicates, with structures that extend through a three-dimensional network of covalent bonds. The structure of

phyllosilicates is based on tetrahedral sheets of cations (commonly Si^{4+}, Al^{3+}, and Fe^{3+}) and octahedral sheets of cations (commonly Al^{3+}, Fe^{3+}, Mg^{2+}, and Fe^{2+}). These layers are classified into 1:1, 2:1 and framework structures. The 1:1 layer is a tetrahedral Si sheet bound covalently to an octahedral Al sheet (Meunier, 2003). A few examples are kaolinite, dickite, and nacrite, which belong to the kaolin group (Brigatti et al., 2006). The 2:1 layer is an octahedral sheet (Al, Mg or Al and Mg) between 2 tetrahedral Si sheets (Meunier, 2003). Examples are montmorillonite, saponite, hectorite, and beidellite, which belong to the smectite group as well as illite, chlorite, and vermiculite (Murray, 2007). Tectosilicates have a three-dimensional framework structure, wherein all the four oxygens of tetrahedron are shared with other tetrahedra (Alaniz et al. 2012); thus, the T-O ratio is 1:2. Examples of tectosilicates include zeolite, quarts, and feldspar (Elliott et al., 2020).

Zeolites

Zeolites (ZEOs) are hydrated aluminosilicates which contain alkali and alkaline-earth metal ions. Natural ZEOs, with a high proportion of clinoptilolite (CLI) (over 80%), are characterized by large specific surface (about 1000 m^2 per g of zeolite), ability to lose or receive water and exchange cations without major changes of the structure, therefore, they have high adsorption capacity for specific mycotoxins. Aluminosilicates are most frequently used for AFs adsorption, although they also bind other mycotoxins, but not so successfully because their hydrophilic surface is less effective in the adsorption of non-polar mycotoxins (Hauschild et al., 2007).

In vitro experiments

According to Bočarov-Stančić et al. (2018) in the *in vitro* tests of mycotoxin adsorption by zeolites, the highest adsorption index was obtained for AFB1 (95.5%) and much lower for T-2 toxin (16.7%) and ZEN (12.2%), while OTA was not bound in applied experimental conditions.

Aluminosilicates modified by the incorporation of long chain organic cations (surfactants) on their surface (organoaluminosilicates) are characterized by increased affinity for non-polar molecules and reduced adsorption of hydrophilic molecules (Pimpukdee et al., 2004). Several research showed that natural zeolite modified organically had higher binding affinity to OTA and ZEN than the unmodified natural zeolite. *In vitro* examinations by Daković et al. (2005) and Daković et al., (2007), showed an increased ZEN adsorption on zeolite modified with different amounts of octadecyldimethylbenzyl ammonium, as compared to the on unmodified zeolite. Furthermore, results obtained by Daković et al. (2007) suggested that ZEN adsorption by organozeolites modified by three different levels (2, 5 and 10 mmol/100g) of octadecyldimethylbenzylammonium, was the result of the adsorption process as well as partitioning. Unlike results obtained *in vitro*, Hauschild et al. (2007) found *in vivo* experiments with piglet's diets contaminated with ZEN (2 mg/kg) that the addition of 0.3% organoaluminosilicate does not affect digestibility of diets and metabolism of pigs.

Research by Marković et al. (2017) revealed that adsorption of OTA and ZEN by ZEO modified with three different levels (2, 5 and 10 mmol/100 g) of benzalkonium chloride (BC), increased, with increasing the amount of BC, but the adsorption mechanism for these two mycotoxins was different. Adsorption of OTA by organozeolites followed nonlinear isotherms

at pH 3 and 7, with higher adsorption capacity at pH 3. On the other hand, adsorption of ZEN showed linear isotherms at pH 3 and 7 and similar amounts were adsorbed at both pH values. According to the authors of the research, this indicates that adsorption was dependent on the form of OTA in solution and that both the sites at the uncovered zeolitic surface and the surfactants contributed to OTA adsorption. ZEN adsorption was independent of the form of ZEN in solution and organic cations at the zeolitic surface were the active sites for ZEN adsorption.

Daković et al. (2010) reported that ZEO modified with octadecyldimethylbenzyl ammonium chloride can bind from 82 to 98% of fumonisin B1 (FB1), depending on the pH. According to these authors, electrostatic interactions between positive uncovered surface and anionic FB1 contributed to the sorption at pH 3. Another *in vitro* experiment with zeolite modified by addition of organic cation, showed that it can adsorb 80.86% OTA in artificial intestinal fluid of broiler chickens (Trailović et al., 2013).

In vivo experiments

In vivo efficacy of zeolites to ameliorate the consequences of aflatoxicosis in poultry has been proven in many studies. Research by Oguz and Kurtoglu (2000) showed that addition of CLI (15 g/kg) to the AF-contaminated diet od broilers (2.5 mg/kg) in the period from 1 to 21 day of age, reduced the deleterious effects of AF on growth performance, i.e. led to the increased food consumption and body weight gain. Higher dietary concentration of CLI (25 g/kg) was less effective and even increased feed conversion ratio, which is possibly a consequence of adsorbent-nutrient interaction. Further research by the group of authors in the similar experiment setting as in Oguz and Kurtoglu (2000), revealed that the addition of 1.5% CLI to broilers' diet, ameliorated the toxic effects of AF (2.5 mg/kg) on serum haematological and biochemical parameters (Oguz et al., 2000) and partially or completely decreased the incidence of affected chickens and the severity of lesions in the organs of chickens (liver, kidneys and thymus) (Ortatatli and Oguz, 2001). Furthermore, addition of CLI (1.5%) into broiler diets contaminated with lower levels AF (50 and 100 ppb), provided significant reduction of the immunotoxic effects of AF (Oguz et al., 2003). Safameher (2008) reported that supplementation of broiler diets with 2% CLI, ameliorated the toxic effect of AF (0.5 ppm) in terms of improved performance, biochemistry parameters and liver histopathology.

In vivo experiments of Vizcarra-Olvera et al. (2012) showed the protective effect of ZEO (0.5 and 1.0 kg per 100 kg) in Bovans chicks fed diet containing 59 mg/kg of FB1 for 3 weeks. Bodyweight improvement was observed, as well as prevention of macroscopic liver lesions and an increase in aspartate aminotransferase activity. Trailović et al. (2013) investigated *in vivo* the effect of the addition of OTA (2 mg/kg) and three different adsorbents: inorganic (modified zeolite), organic (esterified glucomannans) and mixed (inorganic and organic components plus enzymes). The most efficient was the mixed adsorbent which decreased OTA residue concentration by 72.50% in the pectoral muscle and by 94.47% in the liver. Raj et al. (2021) examined the ability of an in-feed modified clinoptilolite zeolite-based mycotoxin binding agent, under commercial name Minazel® Plus, to alleviate gastrointestinal absorption of AFB1 and ochratoxin A (OTA) and its effects on health status and performance of broilers. Results showed that the addition of 2 g/kg of modified ZEO into concurrently AFB1- and OTA- contaminated diets, improved the production performance, i.e. average body

weight gain and feed conversion ratio, glutamate-dehydrogenase level in serum and decreased residue levels of AFB1 in liver and OTA in the spleen of broilers. Pavlak et al. (2023) did not record differences in feed intake, body weight gain and feed conversion ratio, serum levels, intestinal development and litter quality, when zeolite was added to the broilers diet contaminated with lower (FUM 4.2 μg/kg) and higher (FUM, <6.0 μg/kg) mycotoxin level in corn. However, zeolite inclusion at the 5000 g/t or 1000 g/t feed was responsible for the improvement in the percentage of digestible nutrients - crude protein, gross energy and mineral matter. Also, it promoted an increase in hot carcass yield and in the amount of abdominal fat, which can be explained by the temporary connection silicate mineral create with the nutrients, which provides the body with more time to absorb the nutrients present in feed, causing greater protein deposition and consequently higher carcass yield.

Hydrated sodium calcium aluminosilicates

Hydrated sodium calcium aluminosilicate (HSCAS) is considered to be a type of Ca-montmorillonite that has in its structure water molecules bound to a metal centre or crystallized with a complex metal (Kolossova et al., 2009; Di Gregorio et al., 2014). It is naturally occurring or heat-processed and is commonly used as an anticaking additive in animal feed (Wang et al., 2008).

In vitro experiments

Important feature of HSCAS is that it forms a more stable complex with AFB1 than many of the other compounds when tested in vitro (Phillips et al., 1988). Aly et al. (2004) found that HSCAS and the Egyptian montmorillonite (EM) had an excellent capability of *in vitro* adsorbing AFB1 and FB1 in an aqueous solution at different tested levels. The adsorption ratio of HSCAS ranged from 95.3% to 99.1%, and 84.7% to 92.4% for AFB1 and FB1, respectively. EM expressed an adsorption capacity from 95.4% to 99.2%, and 78.2% to 92.2% for AFB1 and FB1, respectively. Both adsorbents were effective at the 0.5% level. High AFB1 adsorption capacity of HSCAS (97.7%) in the solution (pH 8.0) was also reported by Li et al. (2010).

In vivo experiments

Denli and Okan (2006) reported that the addition of HSCAS (2.5 g/kg) to the broiler diets contaminated with 0.40 or 80 μg AFB1/kg, significantly diminished the deleterious effects of AFB1, i.e. the activity of alanine aminotransferase, the weight of livers and histopathological changes induced by AFB1. Girish and Devegowda (2006) observed that, in the experiment with the addition of HSCAS (10 kg/t) in a broiler diet contaminated with AFB1 (1 mg/kg) and T-2 toxin (2 mg/kg), improvement was reflected in weight gain and restored organ weights in the groups fed with AFB1, but not in T-2 toxin fed groups. Addition of 0.15% HSCAS into broilers' feed contaminated with 98.8 μg AFB1 kg-1 resulted in improved growth performance and increased serum protein levels. Neeff et al. (2013) reported the reduction of aflatoxins residues in livers and kidneys of broilers fed diet contaminated with 2.5 mg/kg AFB1, and supplemented with 0.5 kg/100 kg HSCAS for 21 days, but it was not enough to completely prevent the toxic effects of AFB1 in broilers.

The addition of 0.2% HSCAS to the naturally contaminated poultry diet with different concentrations of AFLB1, OTA and T-2 partially improved haematological and biochemical

parameters, hepatic antioxidative status and hepatic injury, except for growth performance (Che et al., 2011). Liu et al. (2018) investigated the effect of lactic acid bacteria (LAB) and HSCAS on detoxification of AFB1 by measuring growth performance, digestibility, immune function, and toxic residues in tissues and excreta of the broiler chickens. LAB and HSCAS were added at 1.5×10^{10} cfu/kg or 3.0 g/kg respectively, to the feed contaminated with 40 μg AFB1/kg. Both LAB and HSCAS supplementation improved the growth performance, immune function and alleviated the damages of AFB1 to kidney and liver, as well as to lymphocytes, but the effect of LAB was greater than that of HSCAS.

Selim et al. (2014) investigated the reduction of AFB1 bioavailability of Nile tilapia fingerlings (*Oreochromis niloticus*). Three adsorbents (HSCAS – 0.5%, *Saccharomyces cerevisiae* and an esterified glucomannan – 0.25%) were used against the feed contaminated with 200 μg/kg AFB1. Supplementation with these adsorbents significantly improved growth performance, blood parameters and immune status, whileAFB1 residues in fish musculature was decreased. HSCAS was the most effective adsorbent in AFB1 toxicity reduction.

HSCAS is characterized as "aflatoxin-selective clay" and is not a good adsorbing agent of other mycotoxins (Phillips, 1999). In order to increase efficiency of the HSCAS for mycotoxins, modification methods were developed. HSCAS adsorbent product, with surface-modified with cetylpyridinium chloride, based on natural bentonite and intercalated with yeast β-glucan, was developed to prevent the harmful effects of T-2 toxin. This modified product is characterized by increased spacing between the particles and the surface of the particles changed from hydrophilic to hydrophobic (Wei et al., 2019). According to Wei et al. (2019), addition of HSCAS (0.05%) modified by cetylpyridinium chloride and the intercalation of glucan, to the basal broiler diet supplemented with T-2 toxin (6.0 mg/kg), improved growth performance, nutrient digestibility and prevented hepatic and small intestine injuries. This indicates that modified HSCAS could be used against T-2 toxin harmful effects in broiler chickens. Furthermore, modified HSCAS proved to be effective in reducing the negative effects of mycotoxins in pigs. Liu et al. (2020a) reported that addition of modified HSCAS to the diet of piglets, at the levels of 1.0 and/or 3.0 mg/kg, alleviated adverse effects of DON on growth performance and improved intestinal microbiota.

Numerous studies aimed to examine the potential of adsorbents to diminish AFB1 transfer rate from feed into its primary oxidized metabolite aflatoxin M1 (AFM1) in cows' milk, since AFM1 is also highly toxic and represents a safety risk in milk and dairy products. Mineral clays, such as activated carbon, zeolite, saponite-rich bentonite, and HSCAS, are able to bind aflatoxins, thus reducing AFB1 absorption in the gastrointestinal tract and its transfer as AFM1 to milk (Giovati et al., 2015; Assaf et al., 2019). In the research by Maki et al. (2016), calcium montmorillonite clay was fed to dairy cows at low and high doses - 0.5 and 1.0% of predicted dry matter intake (DMI), while AF daily dose was 100 μg/kg of the estimated DMI. Results of the research showed that milk AFM1 was reduced from 1.10 μg/L to 0.58 and 0.32 μg/L when 0.5% and 1% of calcium montmorillonite clay was added to the diet, respectively.

Bentonites

Bentonites (BEN), hydrated aluminosilicates from the smectite group, mostly consisting of montmorillonite (50-90%), can also be used for the reduction of mycotoxin levels (Bočarov-

Stančić et al., 2011). *In vitro* and *in vivo* studies show that bentonites are highly effective in the adsorption of aflatoxins (Kong et al., 2014; Rasheed et al., 2020a).

In vitro experiments

Bočarov-Stančić et al. (2018) reported that better *in vitro* binding of ZEN (37.0%) and DON (50.0%) by BEN was observed at pH 3.0, while the reduction of type A trichothecene T-2 toxin was higher at pH 6.9. Bentonite didn't show the ability to bind OTA, but the adsorption index for AFB1 was more than 96%. Kong et al. (2014) used an *in vitro* procedure that mimicked the digestive process in pigs, to investigate the ability of ten toxin binder products, including 5 bentonite clays, to bind or degrade AFB1 and DON. The average percent of adsorption by 5 bentonite clays was 92.5% for AFB1 and only 3.24% for DON.

Wongtangtintan et al. (2015) investigated *in vitro* the adsorption capacity for ZEN of Thai bentonite (TB), and mineral clays (MC). The results indicated that pH 7.0 and 45°C were optimal for ZEN binding and that TB was more effective than the MC in adsorbing ZEN (17.66 mg/g). TB, commercial bentonite (CB) and commercial preparation of activated carbon (AC) were tested for their binding capacities of AFB1 at different temperatures *in vitro* by Wongtangtintan et al. (2016). These authors observed that TB adsorbed AFB1 *in vitro* more efficiently than the other two commercial toxin binders, especially at 25°C.

Chefchaou et al. (2019) investigated the efficacy of 3 different adsorbents: a mixture of two Moroccan clays (calcium BEN and stevensite), Natural Promoter Volatile-NPV (adsorbent based on a combination of clay and essential oils) and commercial preparation Mycofix (based on clays and specific enzymes), for *in vitro* and *situ* mycotoxins' reducing rate in maize flour. All tested binders showed higher AFs adsorption capacity than 70%. The concentration of FUMs decreased at a very low concentration (1 g/kg) of NPV and Mycofix. The maximal inhibitory effect of NPV on DON production (97%) was achieved by 1 g/kg. Non-activated clay was less effective than the treatments with NPV and Mycofix.

Oguz et al. (2022) conducted an extensive study on the *in vitro* mycotoxin binding capacities of mineral adsorbents, glucomannanes and their combinations. They determined and compared the binding abilities of nine different binders (clinoptilolite, sepiolite, bentonite and montmorillonite, glucomannan and four commercial products) on seven different mycotoxins (AF, OTA, ZEA, DON, FUM, T-2 and HT-2 toxin), at pH 3.0 and 6.8 levels, which represent the poultry stomach and intestine environments. Controlled pollution (spike) was created by adding mycotoxins to the clean feed samples, while binders were added to the feed samples to obtain the 0.2% concentration. According to the results of the study, BEN bound AF at 88 or 95%, DON at 23 or 73% and OTA at 54 or 56%, at the pH 3.0 or 6.8, respectively. In general, Oguz et al. (2022) determined that the binding activities of all clays tested *in vitro* on AF, DON, and OTA were higher than those on other mycotoxins.

In vivo experiments

In the research by Kermanshahi et al. (2009) broiler chickens were fed AF contaminated diet (500 and 1000 ppb) supplemented with Na-bentonite (0.5 and 1.0%) during 42 days. According to the results, the addition of Na-bentonite ameliorated negative effect of aflatoxicosis on performance (feed intake, body weight and body weight gain), relative organ weights and on serum biochemistry parameters. *In vivo* experiments of Magnoli et al. (2011)

showed that Na-bentonite decreased histological lesions in the poultry liver caused by 100 μg/kg of AFB1. Protective effect of BEN in Bovans chicks fed with a diet containing 59 mg/kg of FB1 for 3 weeks resulted in body weight improvement, prevention of macroscopic liver lesions and increase in aspartate amino transferase activity (Vizcarra-Olvera et al., 2012).

Besides the negative effects on health, growth and performance, the presence of mycotoxin residues in the livers of poultry represent a threat to the human food chain. In the research by Pappas et al. (2016), four BENs, differing in chemical composition, were used in the *in vivo* experiment, in single or concomitant mycotoxin contamination of chicken diets. Amongst other parameters, the effect of adding BENs to AFB1 and OTA contaminated diets on the amount of mycotoxins in breast muscle and liver was examined. Tissue analysis showed that only OTA was detected and only in the liver and its concentration was 4-fold lower when chickens were fed diet contaminated with AFB1 and OTA at 0.1 mg/kg level, with 0.5% of binder, as compared to the treatment without the binder. This study suggested that AFB1 was metabolised to other non-detectable forms, or it was retained by binder or both and that binder composition and presence of multiple toxins are important factors in terms of binder effectiveness. The carry-over of OTA and AFB1 from feed to tissues varies considerably, depending on the age, breed, and metabolic status of the birds (Khan et al., 2013). Bhatti et al. (2018) evaluated the efficacy of bentonite in reducing the feed-to-tissue transfer of mycotoxins in broiler chickens fed diets contaminated with AFB1 and OTA. They reported 50% reduction in AFB1 levels in the liver of experimental group of broiler chicks, fed AFB1 at 0.1 mg/kg and BN at 3.7 g/kg of feed, while adding BEN at 3.7 and 7.5 g/kg to the feeds contaminated with AFB1 at 0.6 mg/kg resulted in 86% and 87% decrease in AFB1 contents in the liver, respectively. Protective activity of BEN against OTA deposition in liver was also recorded - reduction in OTA contents in the livers of birds fed diet with BEN at the level of 3.7 g/kg and OTA at the level of 0.15, 0.30 and 1.0 mg/kg, was by 62%, 51% and 17%, respectively, as compared to the group without BEN in the OTA-contaminated diet.

Bentonite clay was shown to be effective in reducing carry-over of AFM1 into milk, which is attributed to the binding of AFB1, thus making it unavailable for absorption (Kemboi et al., 2023. Gallo et al. (2020) reported that the addition of 100 g/cow/day bentonite clay into a traditional lactation diet for multiparous lactating Holstein cows, contaminated with 2.13 μg/kg AFB1 (DM basis), reduced the milk AFM1 concentration by 64.8% and had a carry-over reduction of 47.0%.

Diatomite

Diatomite (DIA), the sediment formed in lacustrine and marine environments composed of very small shells of silicon of unicellular algae (*Diatomeae*). It represents a porous material, with high surface area. In addition, this sediment contains the remains of sponges, Radiolaria, admixtures of clay, quartz, etc. (Bočarov-Stančić et al., 2011). If it contains a lot of clay, it is called diatomaceous earth (DAE) (Di Gregorio et al., 2014).

In vitro experiments

In the *in vitro* experiment DIA expressed the best binding capacity for AFB1 (95%) and lower for OTA (66.7%), and T-2 toxin (33.3%) (Bočarov-Stančić et al., 2011). Sprynskyy et al.

(2012) concluded, in the *in vitro* experiment with synthetic gastric and body fluids, that the adsorption of the ZEN on DIA is limited by the competition of less polar toxins with the stronger polar ones.

In vivo experiments

In the research by Modirsanei et al. (2008), the addition of DAE (30 ppm) to AF contaminated broiler diet (1 ppm), ameliorated detrimental effect of AF, i.e., resulted in increased body weight gain, feed intake and improved feed conversion ratio of chickens. In terms of biochemical parameters, DAE supplementation led to increased serum albumin and the activity of serum LDH. Contrary to the results obtained with supplementation of HSCAS, the addition of 2.5 g/kg DAE to the broiler diets contaminated with 40 or 80 µg AFB1/kg failed to prevent harmful effects of AFB1 in terms of histopathological changes (Denli and Okan, 2006). On the other hand, in the research conducted by Lakkawar et al. (2017), addition of 2 g/kg DAE to broilers' feed contaminated with 0.5 and 1 ppm/kg AF, resulted in reduced the severity of lesions in liver and intestines. Pattar et al. (2020) reported that supplementation of DAE at the levels of 0.5 and 1 g/kg to AF and OTA contaminated coloured broilers' feed (0.5 and 1 ppm/kg), led to improvement of body weight gain, feed conversion ratio, feed intake, reduced mortality and ameliorated the pathological changes in the liver.

Pyrophyllite

Pyrophyllite (PYR) is a dioctahedral 2:1 clay mineral of the phyllosilicate group. The hydrophobicity of this mineral is the result of the hydroxyl groups absence on its elementary sheet basal surfaces (Drits et al., 2012).

Under *in vitro* investigation of the mycotoxins adsorption index of PYR, it was found that better results were obtained with a finer granulation sample (≤5µm) than smooth PYR (Marković, 2019). Results were as follows: 84.80/33.45% for AFB1, 33.25/16.55% for ZEN and 2.95/13.05% for OTA for ≤5µm PYR/smooth PYR. The recorded AFB1 binding capacity of this PYR was similar to the adsorption level of this mycotoxin by other aluminosilicate minerals (ZEO, BEN, etc.). According to Fiegenbaum (2019), PYR and HSCAS were proven to have over 80% of AF binding capacity. Patent WO2011023391 is dealing with the adsorbent preparation comprising a clay material and activated carbon that can bind a large variety of toxins, in particular different types of mycotoxins. Besides other clays (natural, synthetic or modified) comprised in the adsorbent, PYR may also be used (Ruf et al. 2012). There are some commercial products with 75% PYR clay and 30% active carbon that assist in binding different toxins including other unwanted microbial by-products (Huang et al. 2016).

Plant-derived mycotoxin adsorbents

Biosorption technology has appeared as a promising alternative to conventional binding technologies (Ringot et al., 2007). It can be performed by biosorbents such as dead biomass, cell and tissue fragments or living cells (bacteria, fungi, yeast and algae) in a metabolically independent process (Fomina and Gadd, 2014). Biosorbents remove contaminants via various physicochemical mechanisms including ion exchange, adsorption, electrostatic attraction, complexation, chelation and micro-precipitation (Volesky, 1994).

Biomass

Studies with plant materials as biosorbents in raw and chemically modified forms confirmed that lignocellulosic wastes are effective in the removal of different toxic materials, including mycotoxins are advantageous over other adsorbents due to immense availability, high adsorption capacity, practicality, low cost, and biodegradability (Adamović et al., 2013; Xu et al., 2016). Disposal of different industrial wastes and by-products containing high amounts of carbon-rich components is considered to be a major problem for the environment. The application of these materials as low-cost effective biosorbents introduces a bifunctional solution from an environmental point of view (El-Sayed and El-Sayed, 2014).

There is a certain number of investigations about the reduction of mycotoxin content *in vitro* by different biosorbents. According to the investigation of Milojković et al. (2012), dried biomass of aquatic weed *Myriophyllum spicatum* had the highest *in vitro* adsorption index for AFB1 (more than 90.0%). The binding capacity for other mycotoxins was less pronounced and varied at different pH values: ZEN (>70.0%), OTA (30.0-50.0%), T-2 toxin (16.7-33.3%). The only non-bound mycotoxin was DON.

Peach and sour cherry peats mechanically treated and acid-treated (0.01 M HCl)) showed different *in vitro* adsorption indexes for five mycotoxins at different pH values: AFB1 (41.1-58.2%), OTA (20.0-76.2%), DON (21.9-50.0%), ZEN (33.3-58.3%) and T-2 (25.0-50.0%) (Stojanović et al., 2012; Lopičić et al., 2013a,b). The better removal was obtained by acid-treated binders, which was expected, having in mind that acid treatment increases specific surface area, as well as type, number, and availability of functional groups responsible for mycotoxins binding. Similar results were obtained by Adunphatcharaphon et al. (2020) who have treated durian peel (DP) with sulfuric acid, to enhance its binding efficiency. The acid-treated durian peel (ATDP) was assessed for simultaneous adsorption of aflatoxin AFB1, OTA, ZEN, DON, and FB1. The results indicated that ATDP exhibited the highest mycotoxin adsorption (not dependable on pH value) towards AFB1 (98.4%), ZEN (98.4%), and OTA (97.3%), followed by FB1 (86.1%) and DON (2.0%).

Avantaggiato et al. (2014) investigated grape pomace (pulp and skin) as a new biosorbent for the reduction of the level of different mycotoxins from liquid media. *In vitro* binding experiments showed that the grape pomace was able to sequester rapidly and simultaneously different mycotoxins. AFB1 was the most adsorbed mycotoxin, followed by ZEN, OTA, and FB1, whereas the adsorption of DON was negligible. The theoretical maximum binding capacities (mmol/kg dried pomace) calculated at pH 7 and 3, were as follows: AFB1 (15.0 and 15.1), ZEN (8.6 and 8.3), OTA (6.3 and 6.9) and FB1 (2.2 and 0.4).

Shar et al. (2016) reported the application of banana peel for *in vitro* removal of five mycotoxins: AFB1, AFB2, AFG1, AFG2 and OTA. AFs binding equilibrium was the highest in the pH range from 6 to 8, while OTA has not shown any significant adsorption due to surface charge repulsion. The maximum monolayer coverage (Q_0) was found to be 8.4, 9.5, 0.4 and 1.1 ng/mg for AFB1, AFB2, AFG1 and AFG2, respectively. The authors concluded that the biosorption of AFs by dried banana peel can be an effective decontamination method for the incorporated mycotoxins in animal feed.

Greco et al. (2019) investigated the ability of 51 agricultural by-products to bind different mycotoxins *in vitro*. These authors found that grape pomaces, artichoke wastes and almond hulls were effective in the adsorption of AFB1, ZEN, OTA and FUMs. For the selected

biosorbents, the calculated maximum binding capacity ranged from 1.2 to 2.9 μg/mg for AFB1, 1.3 to 2.7 μg/mg for ZEN, 0.03 to 2.9 μg/mg for OTA, and 0.01-1.1 μg/mg for FB1, respectively.

Fernandes et al. (2019) characterized the adsorption of AFB1, OTA, and ZEN by dry micronized olive pomace (OliPom) and grape stems (GrapStem). They have compared obtained values with that of three other materials, activated carbon (AC), bentonite (BEN), and a commercial product (ComProd). The strongest adsorbent for OTA and ZEN, was AC (5 mg/ml bound >99%), while ComProd and BEN were the most effective binding agents for AFB1 (0.5 mg/ml bound >95%). Among agricultural by-products, GrapStem was the strongest binder, 10 mg/ml has been sufficient to bind at least 90% of all tested mycotoxins (except OTA at pH 7).

Rasheed et al. (2020b) investigated blueberry and cherry pomace as new biosorbents for aflatoxins (AFs) adsorption from buffered solutions, gastrointestinal fluids and model wine. Blueberry pomace that exhibited the maximum adsorption performance for AFs can be counted as a promising contender for the sequestration of AFSs and other organic pollutants.

In vitro experiments of Nava-Ramírez et al. (2021) were done with two biosorbens - lettuce and field horsetail (0.5% and 0.1% w/v) in removing AFB1 (190 ng/ml). At pH 7, lettuce showed the highest adsorption of AFB1 (95%).

Activated carbon

Activated carbon (AC), the powder formed by pyrolysis of plant materials, is a non-toxic adsorbent of different toxic substances, including mycotoxins.

Döll et al. (2004) found that, contrary to commercially available mycotoxin detoxifying agents and binders as feed additives, AC and cholestyramine were able to bind ZEN and T-2 toxin *in vitro* system that simulated the conditions of the porcine gastrointestinal tract. AFB1 adsorption efficiency (>99%) of AC in aqueous solution (pH 7.0) was demonstrated *in vitro* as well as <99% DON binding by cell culture or intestinal fragments (IPEC-J2) (Di Gregorio et al., 2014).

Kalagatur et al. (2017) applied AC derived from seed shells of *Jatropha curcas* (ACJC) to decontaminate ZEN. The maximum adsorption of ZEN by ACJC was detected as 23.14 μg/mg. According to these authors, ACJC was a potent decontaminating agent for ZEN and could be used as an antidote in the case of ZEN-induced toxicity. The reason for the binding of ZEN by ACJC may be the involvement of the attraction forces between the positive charges of ZEN and the negative ones of ACJC.

Although AC can bind many mycotoxins *in vitro*, including DON (Cavret et al., 2010), its low specificity obtained *in vivo* studies show that it might be saturated with the food matrix components. Therefore, AC is considered to be the most beneficial for minimizing toxin absorption from the GI-tract in acutely exposed animals to toxic substances (Avantaggiato et al., 2004).

Biochars

Biochar has recently gained increasing attention due to its widespread availability, low cost, chemical stability, large specific surface area, high porosity, excellent adsorption performance and biocompatibility (Ying et al., 2021). These exceptional characteristics of

biochars allow their application as the most advanced form of adsorbents in the removal of various pollutants (Hernández-Maldonado et al., 2013). Biochar is made by in the process of thermochemical conversion, which includes pyrolysis, hydrothermal carbonization, gasification and torrefaction (Pang, 2019). Pyrolysis of various types of biomass (renewable material) at temperatures ranging from in an oxygen-free environment under the temperature range of 250−900 °C (Cantrell et al., 2012).

In an *in vitro* study by Ying et al. (2021), a novel adsorbent - biochar for the removal of DON was prepared from soybean dregs. The maximum adsorption capacity of selected biochar to this mycotoxin was 52.99 μg/mg, and the removal efficiency reached 88.31%. Loffredo et al. (2020) evaluated the efficiency of a series of plant-derived biochars for the removal of OTA from water and a water/ethanol mixture. In batch experiments, the highest percentage of removal of the tested mycotoxin in an aqueous solution was shown by wood biochar. Ahmadou et al. (2019) have produced cashew nutshell biochars at different temperatures, T_{pyr} (400, 600 and 800°C) and applied them as a binding agent for AFs and OTA. Results have shown that removal of AFs was very efficient (up to 100% of the toxin's initial value of 20 ng/mL) and independent of operational parameters (pH, stirring speed, T_{pyr}). In opposite, the adsorption efficiency of biochar for OTA increased with the increase of the pyrolysis temperature and stirring speed, while the pH had almost no effect. This kind of biochar can absorb 5 times more AFs than OTA.

Mycotoxin's biosorbents of microbial origin

Yeast cell wall

An interesting alternative to the use of inorganic mycotoxin adsorbing agents and plant-derived products is the use of different microbial products, such as carbohydrate complexes in the yeast cell wall and lactic acid bacteria, that can bind and biotransform mycotoxins (Boudergue et al., 2009). Organic additives such as yeast cell wall and glucomannan have been shown to have a high binding activity across a wide spectrum of mycotoxins compared to inorganic minerals (Kolawole et al., 2019).

In vitro experiments

Freimund et al. (2003) found that 1,3-beta-D-glucan derived from baker's yeast, chemically modified in two steps, showed an excellent binding of ZEN with maximum adsorption (up to 183 mg/g) and relatively high adsorption capacity for trichothecene T-2 toxin (at least 10 mg/g).

Nešić et al. (2009) investigated the adsorption capacity of inorganic (modified clinoptilolite), organic (esterified glucomanane) and mixed adsorbent, which contained inorganic binder, bacteria, enzymes, and well as phytogenic material extracted from plants. All binging agents showed a higher affinity for T-2 toxin in acidic conditions (pH 3.0) which was not significantly differ among tested adsorbents (26.06–34.84%).

Yalcin et al. (2018) investigated adsorption properties of organic, inorganic and mixed toxin binders towards AFB1 under in vitro conditions, at pH 3 and pH 6.8, thus simulating gastrointestinal system of poultry. Inorganic binder included Ca and Al silicates, bentonite, zeolite, sepiolite, clinoptilolite etc., organic binder included cell wall of yeast, glucomannan,

oligosaccharides, organic acid etc., and mixed binder included both. Results of this research showed that inorganic binders' mixture and the mix of organic and inorganic binders were effective in binding of AFB1 (98 and 95% binding activity, respectively), while binding activity of the mixture of organic binders was around 40%.

Kolawole et al. (2019) evaluated and compared the efficacy of ten commercial feed additives to simultaneously bind or adsorb DON, ZEN, FB1, OTA, T-2 and AFB1, which often co-occur in complete feed or feed ingredients. They used an *in vitro* model created to mimic the gastro-intestinal tract of a monogastric animal. Results showed that only modified yeast cell wall effectively adsorbed more than 50% of DON, ZEN, FB1, OTA, T-2 and AFB1, in the following order: AFB1 > ZEN > T-2 > DON > OTA > FB1.

In vivo experiments

Murthy et al. (2002) found that supplementation of feed with glucomannan at 1 kg/ton was beneficial in preventing the absorption of AFB1 and T-2 toxin in the gastrointestinal tract of broiler chickens. Gut contents were collected and analyzed after 0, 30, 60, 90 & 120 minutes of feeding and it was established that glucomannan had the ability to adsorb AFB1 up to 75–90% and T-2 toxin up to 30–35%.

The studies performed with yeast esterified glucomannan (0.5, 1, and 1.5 g/kg) at different concentrations of AF (0.18 mg/kg and 2 mg/kg) in broilers diet (Basmacioglu et al., 2005; Kamalzadeh et al., 2009) showed that glucomannan partially and/or completely diminished the adverse effect of AF on growth performance, biochemical and hematological parameters. Furthermore, the addition of 0.5 and 1 g/kg yeast glucomannan to the broiler diet, contaminated with 2 mg/kg AF, diminished AF induced pathological changes in liver, bursa of Fabricius, thymus, spleen and kidneys. Higher concentration of yeast glucomannan (1 g/kg) was more effective than the lower concentration (0.5 g/kg) and itself had no adverse effect (Karaman et al., 2005). The addition of glucomannan containing yeast product (1 kg/t) in commercial broilers diet contaminated with AFB1 (1 mg/kg) and T-2 toxin (2 mg/kg) was effective in averting the individual and combined toxicity of AF and T-2 toxin (Girish and Devegowda, 2006).

Azizpour and Mogadam et al. (2015) examined the influence of yeast glucomannan and Na-bentonite on serum biochemical parameters and pathological changes in broilers with chronic aflatoxicosis. Broiler feed, contaminated with 250 ppb AF, was supplemented with 0.05 and 0.1% glucomannan and 1.5 and 3% Na-bentonite. It was found that the addition of both adsorbents, alone or in combination, to the aflatoxin-containing diet, reduced the negative effects of aflatoxin. However, supplementation with 0.1% yeast glucomannan alone was more effective than other treatments in ameliorating the adverse effects of aflatoxin.

Probiotics

The binding of mycotoxins through the cell wall components is the most common mechanism of mycotoxin removal by lactic acid bacteria (LAB). It depends on the type of the growth media, bacterial state, type of strain, initial mycotoxin concentration, bacterial count, incubation temperature etc. (Sadiq et al., 2018).

According to recent studies, microorganisms could adsorb 20% to 90% of mycotoxins in different liquid food systems or even body environments (Liu et al., 2020 b).

Among the 5 tested strains of lactobacilli to remove DON and T-2 toxin from Man, Ragosa and Sharpe (MRS) broth of *Lactobacillus plantarum* strain 102 (LP102) showed the strongest ability for that after incubation at 37°C for 72 h. DON and T-2 toxin released from LP102 viable cell-toxin complexes were 28.22±1.55% and 35.42±2.02% of total bound toxins, respectively (Zou et al. 2012). The mode of removal was physical binding, rather than biotransformation.

According to Chlebicz and Śliżewska (2020) all tested strains of *Lactobacillus* sp. (12)-L and *S. cerevisiae* (6)-S detoxified *in vitro* mycotoxins FB1+FUMB2 (max. 77%-L and 74%-S), DON (max. 39%-L and 43%-S), AFB1 (max. 60%-L and 65%-S), T-2 toxin (max. 61%-L and 69%-S) and ZEN (max. 57%-L and 52%-S). These probiotics can potentially be used as additives in animal feed for the reduction of mycotoxin levels (Piotrowska, 2021).

Investigations by Farzaneh et al. (2016) revealed that fengycin and surfactin obtained from *Bacillus subtilis* UTBSP1 can potentially reduce *A. flavus* growth and AFB1 level in pistachio nuts.

Fashandi et al. (2018) reported that the use of LABs, besides their beneficial effects, was a safe method, completely efficient in the removal of the high toxicity effect of aflatoxin M1 in foods having no potential adverse health/toxic effects.

Although some papers are dealing with the AFB1-binding capacity of lactobacilli, there is a growing interest in sterigmatocystin (STC - the precursor of AFs) binding abilities of lactobacilli. Three strains of *L. plantarum* had the best AFB1 adsorption capacities, binding nearly 10% of the mycotoxin present, and in the case of STC, the degree of binding was over 20% (Kosztik et al., 2020).

Polymers

Chitosan (CHI), a non-toxic and biodegradable natural cationic polysaccharide produced from chitin, is the structural element found in the exoskeleton of crustaceans and possesses low immunogenicity. CHI is considered to be a suitable mycotoxin adsorbent with approximately 70% efficacy (Khajarern et al., 2003). CHI solution in a mixture with the minerals rectorite and attapulgite has been patented for removing zearalenone from feed and reducing diarrhoea due to its antimicrobial properties (Huang et al., 2016).

Evaluation of the adsorption capacity of CHI using an *in vitro* digestive model that simulates three gastrointestinal compartments of poultry showed a moderate binding capacity of CHI against five of the six mycotoxins tested, except for DON where only 3.5% was adsorbed (Hernandez-Patlan et al., 2018). This result is in strong interactions of the positively charged CHI at alkaline pH and negatively charged AFB1, FB1, OTA and ZEN. On the other hand, interactions of DON and T-2 with CHI are minor, causing poor binding.

CHI and three cellulosic polymers (HPMC, CMC, and MCC), when tested on six mycotoxins (AFB1, FB1, OTA, T-2, DON, and ZEN) using an *in vitro* digestive model for poultry showed significantly ($p < 0.05$) adsorption capacity against analysed mycotoxins in comparison to the untreated control. HPMC, CMC, and MCC had better binding capacity than CHI (Solís-Cruz et al., 2017).

The large molecular polymers' mass produces unique physical properties for mycotoxin binding and forming a stable complex with them able to pass through the gastrointestinal tract of animals without dissociating AFB1 (Solís-Cruz et al., 2018). These authors evaluated the use

of polymers and probiotics to reduce the AFB1 toxic effect in poultry and obtained highly promising results.

Besides organic polymers (chitosan, cellulose, polysaccharides in the cell walls of yeast and bacteria such as glucomannans, peptidoglycans, etc.), synthetic polymers (cholestyramine and polyvinylpyrrolidone), humic acid and vegetable fibres can also reduce mycotoxin level in feed (Pearce et al., 2010).

In vitro investigations of the elimination of ZEN by two new polymeric forms of cross-linked polyvinylpyrrolidone (PVP) revealed a significant decrease in ZEN concentration from 33.5-66.2% per 25 mg of polymers (Alegakis et al., 1999).

Nanoparticles

Although conventional methods with the application of mineral binders, yeast cell walls, antioxidant additives etc. are at the moment the most widely used products for reducing the impact of mycotoxins, the nanotechnology approach seems to be a promising and effective way to minimize the effects of mycotoxins (Horky et al., 2018).

Carbon nanoparticles

The use of carbon nanostructures is one of the most promising methods for mycotoxin binding. Carbon materials possess high stability, inertness and adsorptive properties, large surface area per weight, and colloidal stability upon various pHs, which is very important for preservation in the gastrointestinal tract (Gibson et al., 2009). According to Chen et al. (2007), carbon nanotube adsorption affinity poorly correlates with hydrophobicity, but increases in the order of nonpolar aliphatic, nonpolar aromatics and nitro-aromatics functional groups.

Fullerenes – a promising class of carbon material, showed higher adsorption capacity than activated carbon (Berezkin et al., 2003). Kovač et al. (2017) found that the concentration of 10 ng/ml of fullerol reduced AF production in an aflatoxigenic strain of *Aspergillus flavus* compared to a control.

Nano-diamonds particles (ND) with an average diameter of about 40 nm, showed that the adsorption capacity for AFB1 is approximately 10 μg/mg and 15 μg/mg for OTA (Puzyr et al., 2007; Gibson et al., 2011). Obtained capacities were higher than those of commercially used clays and yeast cell walls. Adsorption on NDs is related to the size of particles in the case of AFB1, whereas in the case of OTA primarily are important electrostatic interactions that depend on the ND surface functional groups.

Chitosan polymeric nanoparticles

The properties of chitosan polymer and nanoparticles (CHI-NPs) depend on pH, temperature, time and functionalization or modification by specific ligands (Sacco et al., 2016). Glutaraldehyde crosslinked chitosan adsorbed 73% of AFB1, 97% of OTA, 94% of ZEN and 99.5% of FB1 but its binding capacity for DON and T-2 toxin was less than 30% (Zhao et al., 2015).

Clay nanoparticles

Montmorillonite nanocomposites (MN) are perspective adsorbents possessing sizable surface area, higher porosity, strong cation exchange activities, and more active sites, which enable its interaction with mycotoxins (Horky et al., 2018). *In vitro* detected adsorption capacity of MN for AF was 66.67 g/mg MN while *in vivo* testing in broilers demonstrated no toxic effect with a 3 g/kg diet (Shi et al., 2006). Modified nano-montmorillonite by organic cations (cetyltrimethylammoniumbromide) had increased hydrophobicity of the mineral surface and showed a high affinity for AFs, ZEN, and FB1 adsorption in rat models *in vitro* (Horky et al. 2018).

El-Nekeety et al. (2017), investigated the role of organo-modified nano-montmorillonite (OMNM) against the health risk and oxidative stress resulting from exposure of rats to FB1 (50 μg/kg) and ZEN (40 μg/kg) individually or in combination. Co-administration of both mycotoxins indicated a synergistic effect. The authors concluded that OMNM is safe in reduction and/or prevention.

It was shown that stearyldimethylbenzylammonium chloride improves the protective efficacy of halloysite [$Al_2Si_2O_5(OH)_4$] against the harmful effects of ZEN exposure (Zhang et al. 2015).

Metal nanoparticles

Metal nanoparticles (NP) are mainly used because they are stable, act immediately and have the possibility of green synthesis. It is well known that green-synthesized nanoparticles enriched with natural compounds possess better donor activity (Raveendran et al., 2003). According to the investigation of Pietrzak et al. (2015), silver nanoparticles decreased the mycotoxin production of *Aspergillus* sp. (81–96%) and reduced mould cytotoxicity (50–75%).

Polymeric nanocapsules

It is well documented that higher doses of natural antioxidants (tocopherol, selenium, zinc etc.) impact mycotoxin elimination from affected organisms (Horky et al., 2018). Polymeric nanocapsules can protect and deliver these antioxidants to the target tissue where it is gradually released from them. The protective role of chitosan nanoparticles (CHI-NP) with quercetin (Q), a member of the flavonoids family with wide bioactivity (Abbas et al., 2013), was demonstrated against the toxic effect of AFs (Kohli et al., 2002), T-2 toxin (Lesniak-Walentyn et al., 2013), and ZEN (Ben Salem et al., 2015). Round-shaped nanoparticles consisting of quercetin also showed a protective effect on OTA-treated rats (3 mg/kg diet) (Abdel-Wahhab et al., 2017). CHI-NP enhanced the antioxidative activity of Q and protected against OTA induced nephropathy.

Most of the mycotoxin level reduction studies *in vitro* presented in Table 1. mainly investigated the problem of AFs (27%), while *in vivo* studies cited in Table 2. showed that it was the case with FB1 and OTA (27% and 28%, respectively). The obtained result is not surprising having in mind the animal health problems that these mycotoxins can cause.

Nanoemulsions of essential oils

The mycotoxin inhibitory activity of essential oils of thyme, lemongrass, cinnamon, peppermint, and clove was enhanced considerably in nano-emulsion form. The same essential oils exhibited significant differences in inhibition of mycotoxin production in the two *F. graminearum* (Wan et al., 2019).

Conclusions

Features of broad-spectrum mycotoxin adsorbents should be safe, affordable, and nutritionally beneficial to the animal as well as easily included within feed because not all mycotoxin adsorbents have the same capacity to protect livestock against the detrimental effects of mycotoxins. Although *in vitro* tests demonstrate that many mineral substances are effective in mycotoxin adsorption, *in vivo* analysis showed that some of them are not able to protect animals from the toxic effects of these substances.

Zeolites (ZEOs) are efficiently binding AFB1 and FB1 in *vitro* and to some extent ZEN and T-2 toxin. *In vivo* experiment confirmed the protective effect of ZEO in chicks' diets contaminated with FUM as well as OTA. The incorporation of long organic chains in ZEO increased the efficiency in the binding of non-polar molecules, such as ZEN and OTA. **HSCAS's** high adsorption capacity of AFB1 and FB1 was demonstrated *in vitro. In vivo* experiments showed that it is also efficient in the prevention of toxic effects/induced toxicity of AFB1, OTA and T-2 in poultry. Binding preparations of mycotoxins based on **bentonite** (BEN) are more effective in the adsorption of AFLB1 and ZEN than FUMs, DON and T-2 toxin. *In vivo* tests confirmed the protective effect of BEN addition to a poultry diet contaminated with AFLB1 and FB1. **Diatomaceous earth** (DIA) has been shown to have the best capacity for AFB1 adsorption *in vitro* although it can bind to a lesser extent and some other mycotoxins. In opposite, *in vivo* experiments demonstrated that DIA failed to prevent the harmful effects of AFB1 mycotoxin. Although according to a minor number of investigations *in vitro*, **pyrophyllite** possesses the binding ability for some mycotoxins, primary AFB1, it is necessary to continue *in vitro* and to start *in vivo* investigations of its adsorption capacity for different mycotoxins. Even though siliceous substances are efficient binders of AFs, in the case of other mycotoxins their options are very often limited. Also, the chemical composition of them is varying greatly resulting in their different affinities and adsorption capacities for different mycotoxins.

An alternative to inorganic adsorbents can be **plant-derived products**. **Activated carbon** can adsorb *in vitro* many mycotoxins (AFB1, ZEN, T-2 toxin, etc.), but *in vivo* experiments showed that it was not so efficient because of its low specificity. According to *in vitro* tests **biosorbents** are effective in the adsorption of AFB1, ZEN OTA and FB1, whereas the binding of other mycotoxins is negligible. *In vitro* results obtained in experiments with carbohydrate complexes in the **yeast cell wall** revealed that they have the high adsorbing capacities of AFB1, ZEN and T-2 toxin, which were confirmed by *in vivo* tests. **Lactobacilli** remove AFs, STC, DON and T-2 toxin by binding them through cell wall components. **Fungal spores** of some species are capable of AFB1, OTA and ZEN removal. **Chitosan (CHI)** has a moderate adsorption capacity of AFB1, FB1, OTA and ZEN. Interactions of DON and T-2 with

CHI are minor, causing poor binding. By the use of *in vitro* digestive model for poultry, it was shown that **cellulosic polymers** can bind AFB1, FB1, OTA, T-2, DON and ZEN.

Nanotechnology approaches in the reduction of mycotoxins levels seem to be a promising, effective, and low-cost way to minimize the effects of different mycotoxins either by adsorption (more effective for AFs, ZEN, FB1, OTA, and less effective for DON and T-2) or by the decrease of mycotoxin production (AFs, ZEN and DON). *In vivo* experiments showed that particular nanoparticles are safe in the reduction/prevention of harmful effects of AFs, FB1, ZEN and T-2 toxin.

Having in mind that none of the currently applied adsorbents, either mineral compounds or that of biological origin, are effective against all mycotoxins, complete mycotoxin control may require a combination of different approaches with varying modes of action e.g. different combinations of mineral adsorbents, plant-derived products, carbohydrate complexes in the yeast cell wall, probiotics, chitosan, different polymers, etc.

Acknowledgements

This research was financially supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia, contract numbers 451-03-68/2022-14/ 200045 and 451-03-68/2022-14/200023, as well as by the Provincial Secretariat for Higher Education and Scientific Research of AP Vojvodina (Grant number: 142-451-2572/2021-01/01).

Conflicts of interest: None.

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Received: 9 XII 2022

Accepted: 18 IX 2023

Table 1. Studies on the reduction of mycotoxins level in feed by the use of different adsorbent agents *in vitro*

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
MINERAL ADSORBENTs	**Alumino-silicates**	Zeolites (ZEO) modified with octadecyl-Dimethyl benzyl ammonium chloride	FB1	-	-	Differ.t values	-	82-98%	Daković et al. (2010)
		Inorganic modified ZEO (MZEO) Organic esterified ZEO with glucomannans (OZEO)	OTA	- -	- -	- -	- -	Max. 80.86% (MZEO) Max. 74.26% (OZEO)	Trailović et al. (2013)
		ZEO	AFB1 (0.2 μg/ml), T-2 (2.0 μg/ml), ZEN (0.8 μg/ml), OTA (2.0 μg/ml)	K_2HPO_4 buffer	1: 5000	3 and 6.9	-	AFB1 (95.5%), T-2 (16.7%), ZEN (12.2%), OTA was not bound	Bočarov-Stančić et al. (2018)
		Clinoptilolite	AF, OTA, ZEA, DON, FUM, T2, HT2	-	0.2%	3.0 and 6.8	-	AF at 72–90%, DON at 61–	Oguz et al. (2022)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
								68%, and OTA at 52–62%	
	Clays	Bentonites (BEN)	AFB1 (0.2 μg/ml), DON (2.0 μg/ml), T-2 (2.0 μg/ml)	K_2HPO_4 buffer	1: 5000	3 and 6.9	-	AFB1 (>95.0%), DON (50.0%), T-2 (>25.0%)	Bočarov-Stančić et al. (2011)
		Thai bentonite (TB)	ZEN (4 μg/ml)	At 45°C	-	7	17.66 mg/g		Wonghtangtintan et al. (2015)
		Commercial bentonite (CB) Activated carbon (AC) TB	AFB1 (5 mg/l)	-	-	-	-	More efficient TB at 25°C than CB and AC	Wonghtangtintan et al. (2016)
		Bentonites (BEN)	AFB1 10 ng/ml DON 250 ng/ml	2 h in shaking incubator at 39°C	0.5%	2	-	average adsorption AFB1 92.5% DON 3.24%	Kong et al. (2014)
		Bentonites (BEN)	AF, OTA, ZEA, DON, FUM, T2, HT2	-	0.2%	3.0 and 6.8	-	BNT bound AF at 88–95%, DON at 23–73%, and OTA at 54–56%	Oguz et al. (2022)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
		Moroccan clay (MC) Natural promoter volatile (NPV)	Total AF (26.2 μg/kg) DON (16.3 mg/kg)	Simulated the conditions of the gastrointe stinal tract of pigs	2 g/kg 1 g/kg	6.8	-	71.8% 97%	Chefchaou et al. (2019)
		Diatomite (DIA)	AFB1 (0.2 μg/ml), T-2 (2.0 μg/ml), OTA (2.0 μg/ml)	K_2HPO_4 buffer	1: 5000	3 and 6.9	-	AFB1 (95.0%), T-2 (33.3%), OTA (66.7%)	Bočarov-Stančić et al. (2011)
			ZEN	Synthetic gastric fluid (SGF), Synthetic body fluid (SBF)	-	-	-	53% (SGF), 42% (SBF)	Sprynskyy et al. (2012)
		Pyrophyllite (PYR) Finer granulation of ≤5μm (FG), Smooth (S)	AFB1 (2 mg/l), ZEN (2 mg/l), OTA (2 mg/l)	Phosphate buffer	5 mg	5	AFB1(1.7-FG, 0.7-S, mg/g), ZEN (0.7-FG, 0.3-S, mg/g), OTA (0.3-FG, 0.06-S, mg/g)	AFB1 (84.8%-FG, 33.4%-S) ZEN (33.35%-FG, 16..6%-S) OTA (13.0%-FG, 3.0%-S)	Marković (2019)
PLANT-DERIVED PRODUCTS	**Biomass**	Aquatic weed *Myriophyllum spicatum*	AFB1 (0.2 μg/ml), DON	K_2HPO_4 buffer	1:5000	3 and 6.9	-	AFB1 (>90%), DON (0%),	Milojković et al. (2012)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
			(2.0 μg/ml), ZEN (0.8 μg/ml), OTA (2.0 μg/ml), T-2 (2.0 μg/ml)					ZEN (>70.0%), OTA (>30.0), T-2 (>16.7),	
		Peach pits	AFB1 (0.2 μg/ml), DON (2.0 μg/ml), ZEN (0.8 μg/ml), OTA (2.0 μg/ml), T-2 (2.0 μg/ml)	K_2HPO_4 buffer	1:5000	3 and 7	-	AFB1 (>41.2%), DON (>23.1%), ZEN (>33.3%), OTA (>33.2%), T-2 (>25%)	Lopičić et al. (2013a)
		Sour cherry pits	AFB1 (0.2 μg/ml), DON (2.0 μg/ml), ZEN (0.8 μg/ml), OTA (2.0 μg/ml), T-2 (2.0 μg/ml)	K_2HPO_4 buffer	1:5000	3 and 7	-	AFB1 (>41.2%), DON (>21.9%), ZEN (>33.3%), OTA (>20.0%), T-2 (>40%)	Lopičić et al. (2013b)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
		Grape pomace	AFB1, ZEN, OTA, FB1	-	-	3 and 7	AFB1 (15.0 - 15.1 mmol/kg), ZEN (8.6 - 8.3 mmol/kg), OTA (6.3-6.9 mmol/kg), FB1 (2.2 - 0.4 mmol/kg)	-	Avantaggiato et al. (2014)
		Grape pomaces, Artichoke wastes, Almond hulls	AFB1 (1 μg/ml), ZEN (1 μg/ml), OTA (1 μg/ml), FB1 (1 μg/ml)	Citrate and phosphate buffer	1 mg/ml	3 and 7	AFB1 (1.2-2.9 μg/mg), ZEN (1.3-2.7 μg/mg), OTA (0.03-2.9 μg/mg), FB1 (0.01-1.1 μg/mg)	-	Greko et al. (2018)
		Dry micronized olive pomace (OliPom), Grape stems (GrapStem)	AFB1, OTA, ZEN	-	30 mg/ml 10 mg/ml	2 and 7	-	Less efficient All, except OTA at pH 7.0 (>90%)	Fernandes et al. (2019)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
		Lettuce, Field horsetail,	AFB1 (190 ng/ml)	-	0.5 and 0.1 w/v	2, 5 and 7	-	With 0.5% w/v all biosorbents (70-100%), With 0.1 w/v, at pH 7.0 lettuce (95%)	Nava-Ramírez et al. (2021)
	Activated carbon (AC)	AC	AFB1 (0.821 µg/ml)	-	82 mg/ml	7	-	>99%	Di Gregorio et al. (2014)
	Biochars	Biochar soybean dregs prepared with activator KOH	DON (30-90 µg/ml)	At 35°C	1.0 mg/ml	3-8	52.9877 µg/mg	88.31% at 318 °K	Ying et al. (2021)
		Biochar of Cashew nutshell (400, 600 and 800°C)	AFs (180 ng/ml) OTA (38 ng/ml)	Filtration or steaming	25 mg/ml	4.15, 6.54 and 9.05	-	AFs (100%), OTA (29-52%)	Ahmadou et al. (2019)
		Wood biochar	OTA (1mg/l)	-	2.0 mg/ml	6.3	500 mg/kg	100%	Loffredo et al. (2020)
MYCOTOXIN'S BIOSORBENTS OF MICROBIAL ORIGIN	**Yeast cell wall**	Glucomannan (esterified)	T-2 (1 mg/ml)	in buffer solution at 37°C during 1 h	100 mg	3 7	-	34.84% 29.76%	Nešić et al. (2009)
		Glucomannan (esterified)	AFB1 (21.2 µg/kg), OTA (48.9 µg/kg), DON (997.2 µg/kg), FB1 (5582.3 µg/kg),	40 °C 100 rpm 270 min	20 mg on 1 g of contaminated feed	60 min at pH 4.5–5.3, 90 min at pH 1.9–3.7,	-	AFB1 (39%), OTA (26%), DON (36%), FB1 (19%),	Kolawole et al. (2019)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
			T-2 (243.1 µg/kg), ZEN (152.8 µg/kg)			120 min at pH 5.3–7.5		T-2 (00%), ZEN (41%)	
		Glucomannan	AFB1 (21.2 µg/kg), OTA (48.9 µg/kg), DON (997.2 µg/kg), FB1 (5582.3 µg/kg), T-2 (243.1 µg/kg), ZEN (152.8 µg/kg)	40 °C 100 rpm 270 min	20 mg on 1 g of contaminated feed	60 min at pH 4.5–5.3, 90 min at pH 1.9–3.7, 120 min at pH 5.3–7.5	-	AFB1 (54%), OTA (29%), DON (47%), FB1 (45%), T-2 (28%), ZEN (40%)	Kolawole et al. (2019)
		Modified yeast cell wall	AFB1 (21.2 µg/kg), OTA (48.9 µg/kg), DON (997.2 µg/kg), FB1 (5582.3 µg/kg), T-2 (243.1 µg/kg), ZEN (152.8 µg/kg)	40 °C 100 rpm 270 min	20 mg on 1 g of contaminated feed	60 min at pH 4.5–5.3, 90 min at pH 1.9–3.7, 120 min at pH 5.3–7.5	-	AFB1 (62%), OTA (52%), DON (55%), FB1 (51%), T-2 (56%), ZEN (53%)	Kolawole et al. (2019)
	Probiotics	*Lactobacillus plantarum* (LP102)	DON (1.0 µg/ml), T-2 toxin (1.0 µg/ml)	At 37°C for 72 h	1.0 µl/ml	7.4	-	28.228%, 35.42%	Zou et al. (2012)
POLYMERS	**Organic polymers**	Chitosan (CHI)	AFB1, FB1., OTA, T-2, DON, ZEN	Digestive model for poultry	-	-	-	>35%, >30%, 50%, >20%, 3.5%. >70%	Hernandez-Patian et al. (2018)
NANO-PARTICLES (NP)	**Carbon NP**	Diamond NP (about 40 nm)	AFB1 or OTA (10 µg/mg)	-	0.1 %	-	-	12% (AFB1), ≥20% (OTA)	Gibson et al. (2011)

Type of binding agent	Group	Adsorbent agent	Mycotoxins' concentration	Experiment conditions	Addition of the agent	pH	Adsorption capacity	Adsorption efficiency	References
	Chitosan polymeric NP	Cross-linked chitosan-glutaraldehyde complex	AFB1, OTA, ZEN, FB1, DON, T-2	-	15 μg/mg	-	-	73%, 97%, 94%, 99.5%, <30%, <30%	Zhao et al. (2015)

Table 2. Studies on the reduction of mycotoxins levels in feed by the use of different binding agents *in vivo*

Type of binding agent	**Group**	**Adsorbent agent**	**Mycotoxins concentration**	**Animals**	**Addition of the agent**	**Effects of toxin reduction**	**References**
MINERAL ADSORBENTS	**Alumino-silicates**	Inorganic modified zeolites (MZEO), Organic esterified glucomannans (OZEO), Mixed MZEO and OZEO plus enzymes)	OTA	Broilers during 21 days	2 mg/kg	Decreased residue concentration by 72.50% in pectoral muscle and 94.47% in liver	Trailović et al. (2013)
		Zeolites (ZEO)	FB1 (59 mg/kg)	Bovans chicks diet during 3 weeks	0.5 and 1.0 kg per 100 kg	Bodyweight improvement as well as prevention of macroscopic liver lesions and increase in	Vizcarra-Olvera et al. (2012)

						aspartate aminotransferase (AST) activity	
		Zeolites (ZEO)	FUM (4.2 µg/kg and 6.0 µg/kg)	Broilers	5000 g/t or 1000 g/t	improvement in the digestibility of nutrients increase in hot carcass yield and in the amount of abdominal fat	Pavlak et al. (2021)
		Clinoptilolite	AF (2.5 mg/kg)	Broilers	1.5% and 2.5%	reduction of deleterious effects of AF on growth performance moderate decrease of affected broilers and/or the severity of lesions reduction of toxic effects of AF on serum haematological and biochemical parameters	Oguz and Kurtoglu (2000) Ortatatli and Oguz (2001) Oguz et al. (2000)
		Clinoptilolite	AF (50 and 100 ppb)	Broilers	1.5%	significant reduction of the immunotoxic effects of AF	Oguz et al. (2003)
		Clinoptilolite	AF (0.5 ppm)	Broilers	2%	improved performance, biochemistry parameters and liver histopathology	Safameher (2008)

		Modified clinoptilolite zeolite (ZEO)	AFB1 (0.02 and 0.05 mg/kg feed) OTA (0.1 and 0.5 mg/kg feed)	Broiler chickens (Cobb 500)	1 and 2 g/kg feed	significantly decreased residue levels of AFB1 in liver and OTA in the spleen	Raj et al. (2021)
	Clays	Bentonites (BEN)	AFB1 (100 µg/kg)	1 day old male Cobb chicks	0.3%	Decreased histological lesions in the poultry liver caused by AFB1	Magnoli et al. (2011)
			FB1 (59 mg/kg)	Bovans chicks		Bodyweight improvement, prevention of macroscopic liver lesions and increase in AFS activity	Vizcarra-Olvera et al. (2012)
		Bentonites (BEN)	AFB1 (2.13 µg/kg, DM basis)	Dairy cows	100 g/cow/day	BEN reduced the milk AFM1 concentration by 64.8% and had a carry-over reduction of 47.0%	Gallo et al. (2020)
		Bentonites (BEN)	AFB1 (0.1, 0.2 and 0.6 mg/kg) OTA (0.15, 0.3 and 1.0 mg/kg)	Broilers	3.7 and 7.5 g/kg 3.7, 7.5 and 15 g/kg	50% reduction in AFB1 levels in the liver up to 62% of OTA reduction in the liver	Bhatti et al. (2018)
		Bentonites (BEN)	AF (500 and 1000 ppb)	Broilers	0.5 and 1.0%)	Reduction of negative effect of AF on	Kermanshahi et al. (2009)

						performance, relative organ weights and on serum biochemistry parameters	
		Calcium montmorillonite clay	AFB1 (100 µg/kg of the estimated dry matter intake)	Dairy cows	0.5 and 1.0% of predicted dry matter intake	milk AFM1 was reduced from 1.10 µg/L to 0.58 and 0.32 µg/L	Maki et al. (2016)
		Diatomite (DIA)	Combined AF and OTA (0.5 and 1 mg/kg)	Coloured broiler (RAJA II) chickens	0.5 and 1 g/kg	improvement of body weight gain, feed conversion ratio, feed intake, reduced mortality and ameliorated the pathological changes in the liver	Pattar et al. (2020)
		Diatomite (DIA)	AFB1 (40 or 80 µg/kg)	Broilers	2.5 g/kg	DIA failed to prevent the harmful effects of AFB1	Denli and Okan (2006)
		Diatomite (DIA)	AFB1 (1 ppm)	Broilers	30 ppm	increased body weight gain, feed intake and improved feed conversion ratio of chickens. Increased serum albumin and the activity of serum LDH	Modirsanei et al. (2008)
	Clay nanoparticles	Montmorillonite organo modified (OMNM)	FB1 (50 mg/kg b.w.),	Rats	5 g/kg diet	OMNM alone was safe and succeeded to reduce and/or	El-Nekeety et al. (2017)

			ZEN (40 µg/kg b.w.), FB1+ZEN			preventing most of the toxicity of FB1 and ZEN	
		Halloysite (MHNT)	ZEN (2.77 mg/kg)	Sow and piglets	1%	The MHNTs significantly reduced the damage to the fat in the colostrum and the protein, and lactose in the milk induced by the ZEN-contaminated feed	Zhang et al. (2015)
MYCOTOXIN'S BIOSORBENTS OF MICROBIAL ORIGIN	**Yeast cell wall**	Glucomannan	AFB1 (250 and 500 ppb) T-2 toxin (500 and 1000 ppb)	Broilers	0.1 %	Adsorption: AFB1 up to 75–90% T-2 up to 30–35%	Murthy et al. (2002)
		Glucomannan (esterified)	AF (0.18 and 2 mg/kg)	Broilers	(0.5, 1, and 1.5 g/kg)	partially and/or completely reduction of the adverse effect of AF on growth performance, biochemical and hematological parameters	Basmacioglu et al. (2005) Kamalzadeh et al. (2009)
		Glucomannan	AF (2 mg/kg)	Broilers	(0.5 and 1 g/kg)	reduction of AF induced pathological changes in liver, bursa of Fabricius, thymus, spleen, and kidneys	Karaman et al. (2005)

		Glucomannan	AFB1 (1 mg/kg) T-2 (2 mg/kg)	Broilers	1 kg/t	reduction of the individual and combined toxicity of AF and T-2 toxin	Girish and Devegowda (2006)
		Glucomannan	AF (250 ppb)	Broilers	0.05 and 0.1% glucomannan	reduction of the negative effects of aflatoxin	Azizpour and Mogadam et al. (2015)
POLYMERIC NANO-CAPSULES		Quercin (Q)	OTA (10 mg /kg diet)	Rats	100 mg/kg	Q had no impact on the toxicokinetics of OTA i*n vivo*	Abbas et al. (2013)
		Quercin (Q)	T-2 toxin (0.08 mg/kg BW)	Rabbits	1 mg/kg BW	Q reduced cell apoptosis and had the potential to attenuate T-2 toxin-induced proliferation arrest	Lesniak-Walentyn et al. (2013)
		Chitosan (CHI), plus Q	OTA (3 mg/kg diet)	Rats	140 mg/kg BW or 280 mg/kg BW, 50 mg/kg BW	Severe histopathological and serum changes, as well as other toxicological effects of OTA, were successfully overcome with the additional combination of Q and higher doses of CHI	Abdel-Wahhab et al. (2017)