



DETOXIFICATION IMPACTS OF DIETARY PROBIOTIC AND PREBIOTIC SUPPLEMENTS AGAINST AFLATOXINS: AN UPDATED KNOWLEDGE – A REVIEW

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Abstract

The widespread prevalence of food pollutants seriously threatens human and animal health. Mycotoxins are secondary metabolites primarily formed by toxigenic fungal genera, including *Aspergillus*, *Penicillium*, *Fusarium*, and *Alternaria*, demonstrating one of the principal pollutants in diets or feed products. Mycotoxin contamination in food can harm health, including stunted development, immune system suppression, infertility, vomiting, and gastrointestinal and cancerous conditions. These effects can occur both acutely and chronically. The complex food chain can be contaminated with mycotoxins at any point, including during harvest, industrial processing, shipping, or storage, putting the food sector under societal pressure owing to the waste generated by infected goods. One of the biological controls of mycotoxin is provided by probiotics and prebiotics, controlled as foods and dietary supplements made of bacteria or yeast. Aflatoxin's bioavailability and gastrointestinal absorption can be reduced using various probiotics and prebiotics.

Key words: probiotics, prebiotics, mechanism of action, aflatoxin, detoxification, animal health

Foodborne microbiota infection causes significant amounts of the world's food production to deteriorate (Muhialdin et al., 2020). Besides, the fungus is one of the main reasons damaged food and ill systems affect people. As well as, since 5% to 10% of the world's food output is thought to be lost owing to fungal infection, fungi play a substantial part in spoiling food components (Abdel-Wahhab et al., 2005; Saeed et al., 2017). Meanwhile, the feeding products' financial value, dry matter, and quality decrease due to the growth and survival of these fungi (Abdelmotilib et al., 2018).

Mycotoxins, toxic substances damaging to human and animal health, may be created if the fungus develops on a food product. Because of this, fungi and harmful compounds must be reduced or eliminated. Doing so will assist the world's health and also help to prevent food loss and instability (Jiang et al., 2018; Eskola et al., 2020). The presence of several biological poisons in the environment threatens the health of both people and animals. However, mycotoxins are the most dangerous since they can harm people and animals and cause a variety of ailments. It is a secondary metabolite that originates from fungi. Most filamentous fungi species that produce

it are *Aspergillus* spp., *Fusarium* spp., and *Penicillium* sp. (Marchese et al., 2018).

Mycotoxin is a term used to describe foods and dietary supplements made of yeast or bacteria that are regulated. Probiotics are a biological control for mycotoxin. They are available in capsulated forms, pills, sachets, or powders and may be found in various fermented foods, most typically yogurt or dairy products. One bacterial species or a combination of multiple species may be present in products containing probiotics. Thus, probiotics are defined as "live microorganisms that, when supplied in sufficient proportions, impart health advantages on the host" by the World Health Organization (WHO) working groups. Probiotic bacteria used in food applications can come from either food (artisanal fermented goods) or humans (feces, breast milk) (Alpsoy and Yalvac, 2011). Likewise, many feed additives, such as prebiotics, probiotics, and botanical components, have been proposed over time and, in certain circumstances, used to produce alternative and organic poultry (Ricke, 2015; Abd El-Aziz et al., 2022; Abd El-Hack et al., 2022).

According to Guan et al. (2021), using microbes is particularly efficient, inexpensive, secure, and ecologi-

cally friendly. This is especially true of microorganisms having probiotic qualities. Removing chemical pesticides and contaminants from food and feed and lacking harmful residues are the pleasing fruits of bacterial detoxification. Likewise, Solis-Cruz et al. (2019) evaluated the use of probiotics and polymers to lessen the toxic impacts of AFB1 in poultry. They discovered that adding non-nutritional adsorbents to the diet can help poultry avoid developing aflatoxicosis by binding AFB1 in the gastrointestinal tract.

Prebiotics and/or probiotics have a crucial role in reducing toxins being reduced in agricultural goods (El-Shall et al., 2019; Arif et al., 2020). This makes it fascinating, and probiotics and prebiotics are paying more attention to toxins reduction, which is currently a researchable topic. The present review article aimed to assess the effects of probiotics and prebiotics on mycotoxin and aflatoxin reduction mechanisms.

Probiotics

The word “probiotic” was first used in 1906 by Elie Metchnikoff, who received the Noble Prize in medicine. He displayed how treating intestinal diseases may include replacing bad bacteria with beneficial ones. Therefore, he is considered the founder of probiotics (Ricke, 2015). Probiotics are also known as “direct-fed microbials”, and they help the host by keeping the populations of gut microorganisms in balance (Wondwesen and Moges, 2017; Rehman et al., 2020; Yaqoob et al., 2021). Additionally, probiotics were originally thought to include substances that promoted one another. The expression is utilized animal feed additives to look into favorable effects. Probiotics are helpful bacteria that, when provided in sufficient amounts, have a good result on the host’s body, according to the Food and Agriculture Organization (FAO) and WHO (Hotel and Cordoba, 2001).

The International Scientific Association approved this definition for probiotics and prebiotics (Jiang et al., 2008). Probiotics have various forms, including yeast, single or multiple species, allochthonous, and autochthonous bacteria (spore-forming or non-forming). Additionally, among the bacteria usually used as probiotics are *Lactobacillus*, *Enterococcus*, *Streptococcus*, *Clostridium*, *Bacillus*, *Bifidobacterium* spp., *E. coli*. *Aspergillus oryzae* and *Saccharomyces cerevisiae* are two examples of yeast and fungus utilized as probiotics (Wondwesen and Moges, 2017).

Also, yeast and bacteria are used as living microorganisms or as spores. While *Lactobacillus* and *Enterococcus* spp. are colonizing species, *S. cerevisiae* and *Bacillus* spp. (spores) are not. *Saccharomyces* is a probiotic organism well known for supplying B complex vitamins and high-quality protein. Probiotics enhance metabolism, sustain bird health, aid in better digestion, and hasten chicken weight gain (Wondwesen and Moges, 2017).

A minor number of facultative anaerobic bacteria exist in the small intestine and the crops, proventriculus, and gizzard among probiotic microorganisms, respec-

tively (Khan et al., 2020). The enterocyte, caecal, and colonic epithelium are all colonized by probiotic bacteria, with the colon and caecum having the highest colony densities (10^{10} – 10^{13} cfu/g) (Ricke, 2015).

Prebiotics

Prebiotics are challenging to characterize in a few words. Still, they all have the same basic function: they improve the host animal’s health by increasing the proliferation, metabolism, and composition of helpful natural microorganisms in the gastrointestinal tract (GIT) while removing harmful ones. Prebiotics are fed as components in feed, but they cannot be absorbed since they cannot be broken down by enzymes (Ricke, 2018). Furthermore, prebiotics generally have these characteristics in common. Still, they also share some other traits, such as alterations to the GIT microbiome for a healthy structure, manipulation of the animal host defensive system, tolerance to stomach acidity, selective fermentability via a few amounts of potentially favorable microorganisms (Bandyopadhyay et al., 2016).

Prebiotic candidates were previously restricted to carbohydrate additives, such as oligosaccharides and non-starch polysaccharides. Yet, today the description of prebiotics has been expanded to include “a substrate that is selectively utilized by host microorganisms conferring a health benefit”, meaning that a variety of polyphenols and poly-unsaturated fatty acids, as well as oligosaccharides with various lengths of carbon chains, may fit the bill (Gibson et al., 2017). Accordingly, to inhibit pathogen colonization and GIT health, a wide variety of prebiotic alternatives have been tested in aviculture. However, they have been defined primarily, revealing their origin, pureness, chemical properties, structure, proper dosage, and possible side effects. These include mannan oligosaccharides, inulin and fructo- oligosaccharides, galacto- and xylo-oligosaccharides, and isomalto-oligosaccharides. Besides, some other carbohydrates of non-starch polysaccharides, like β -glucan, are among the most often utilized prebiotics in poultry feed (Slawinska et al., 2019). It might also be given *in ovo* at a concentration at least ten times lesser than that after hatching, resulting in the same positive impacts as an oral treatment. This prebiotic is typically given to chickens orally within the first few days or hours of hatching, either by directly spraying it into the feed or adding it to the drinking water (Slawinska et al., 2019).

As previously mentioned, prebiotics’ principal role is to change the intestinal flora in a good way for the host, with beneficial impacts both within the intestinal lumen and throughout the body. This is demonstrated by improvements in productive parameters like body weight gain, egg production, rate of feed conversion, and mortality index (Li et al., 2008). Moreover, prebiotics have demonstrated their efficiency in decreasing pathogenic colonization by *E. coli*, *Campylobacter*, *C. perfringens*, and *Salmonella*, improving host health and productivity (Kim et al., 2019). Accordingly, prebiotics are a great

option because of this collection of favorable benefits, as well as the lesser chances of negative host side effects and being more affordable and practical to produce in large quantities than probiotics. Prebiotics are a better substitute for probiotics that help poultry producers use fewer antibiotics, which will aid in addressing the problem of antimicrobial resistance (Clavijo and Flórez, 2018).

Aflatoxin

Specifically, mycelial filamentous entities known as molds create mycotoxins as secondary metabolites (Jiang et al., 2018). The most widely distributed mycotoxins, including aflatoxins (AFs), ochratoxin, zearalenone, deoxynivalenol, and trichothecene-2, are made by *Aspergillus* sp., *Fusarium* sp., and *Penicillium* spp. (Binder et al., 2007; Bandyopadhyay et al., 2016). Hence, aflatoxin represents the well-investigated mycotoxin found in agricultural products. *Aspergillus flavus*, *A. nomius*, and *A. parasiticus* are the principal producers of aflatoxin. In humans, AFs have been shown to cause immunological suppression, nephron toxicity, and liver damage (Winter and Pereg, 2019). Furthermore, AFB1 is the most dangerous of the AFs and is regarded as a Group I naturally produced carcinogen (Khan et al., 2020). Furanocoumarins, known as AFs, are composed of coumarin and either a cyclopentanone or a lactone in place of a bisdihydrodifuran or tetrahydrofuran. The toxic and carcinogenic properties of AFs are due to the ring structure and the dual bonds in the terminating furan ring (Nazhand et al., 2020).

Aspergillus flavus and *A. parasiticus* are thought to form aflatoxins, among the most harmful mycotoxins (Ehsani et al., 2016). Additionally, these toxins have negative consequences such as toxicity, carcinogenicity, mutagenicity, teratogenicity, and immunosuppression (Mottaghianpour et al., 2017). Additionally, these genotoxic substances target several organs including the liver, kidneys, and immune systems. Their signs include liver cancer, necrosis, fatty liver, anorexia, diarrhea, and vomiting. Their effects on reproduction involve delayed testicular growth, reduced testosterone plasma level, and decreased live sperm percentage. Increased susceptibility to secondary infection by parasites such as fungi or bacteria is another result of their immunosuppressive properties. Encephalopathy and interstitial fibrosis are other associated symptoms (Krska et al., 2012).

Aflatoxicosis affects growing animals, including calves, dogs, young pigs, pregnant sows, and fowl (particularly ducklings and turkey poults). All studied animal species in experiments have displayed some level of vulnerability. Aflatoxin levels in the diet typically tolerated in chicken are 50.0 ppb for young birds and 100.0 ppb for adult ones. Aflatoxin concentrations two times higher than these levels are likely to result in clinical illness, including some mortality (Zhang et al., 2019).

The liver converts aflatoxins into an epoxide, which has a strong affinity for nucleic acids and nucleopro-

teins. Due to nuclear DNA's alkylation (Hathout and Aly, 2014), they can cause mutagenesis, cancer, teratogenesis, decreased protein synthesis, and immunosuppression, among other harmful effects. The production of vital metabolic enzymes and growth-promoting structural proteins is decreased because of decreased protein synthesis. The main organ in question is the liver. Aflatoxin exposure at high doses causes hepatic necrosis; exposure at low doses for a long time reduces the growth rate, suppresses the immune system, and enlarges the liver (Ślizewska et al., 2019).

Changes in hematological and biochemical parameters affect metabolism by altering the enzyme pathways of carbohydrates, lipids, proteins, and nucleic acids, with serious consequences for livestock and human. As a result, the activity of the serum enzymes glutamate pyruvate transaminase, glutamate oxaloacetate transferase, and glutamyl transferase rises, causing immunosuppressive effects, hepatotoxic, cancerous, mutagenic, and teratogenic, as well as the possibility of death in cases of severe intoxication (Zinedine and Mañes, 2009; Yunus et al., 2011). In chickens, chronic or acute aflatoxicosis causes liver and intestinal damage in addition to development retardation, poor egg quality and production, immune system impairment, and increased mortality (Danicke et al., 2002; Pandey and Chauhan, 2007). Acute aflatoxicosis is typically linked to aflatoxin contents in the feed that exceed the acceptable values mentioned above. Decreased clotting factor production due to liver injury can occur with acute and chronic bleeding. Despite immunization, subclinical consequences include hypoproteinemia, decreased resistance to several viral illnesses, and decreased growth rates and feeding efficiency (Huang et al., 2020).

Types of aflatoxins

Four aflatoxins were generated by *A. parasiticus*, *A. flavus*, and *A. nomius*, identified as Aflatoxin B1, B2 (AFB1, AFB2) and Aflatoxin G1, G2 (AFG1, AFG2), which are among the primary members of the 18 different forms of aflatoxins that have been found (Abd El-Hack et al., 2018; Amer et al., 2018). Nonetheless, in human and animal milk fed on spoiled food, there are Aflatoxin M1, M2 (AFM1, AFM2) metabolites of AFB1 and AFB2. The most toxic among other species is AFB1. Other species that can produce aflatoxin include *A. ochraceoroseus*, *A. toxicarius*, *A. pseudotamarii*, and *A. rambellii* (Reiter et al., 2009). Additionally, other *Aspergillus* fungi (such as *A. carbonarius* and *A. ochraceus*) produce ochratoxin A (OTA), a significant mycotoxin (Sarigiannis et al., 2014; Agriopoulou et al., 2016). *A. parasiticus* and *A. flavus* generate AFB1 rather than AFG1 and come in a range of toxic and non-toxic forms. *A. parasiticus* is made up of varied concentrations of AFB1, AFB2, AFG1, and AFG2, all of which have varying levels of toxigenicity. Aflatoxins B are considered more toxic than Aflatoxins G and appear more commonly as a pollutant (Jw, 2003).

Table 1. Chemical composition, toxic groups, biological consequences of the principal mycotoxins, and generating fungi

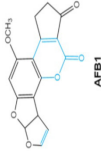
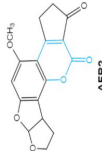
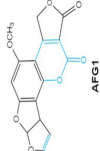
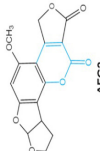
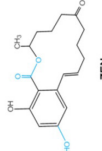
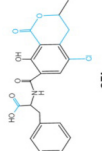
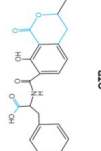
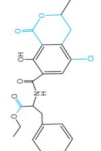
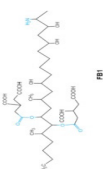
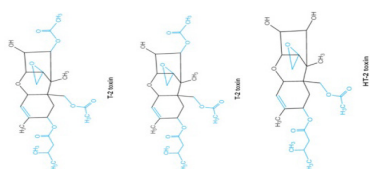
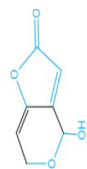
Mycotoxin	Chemical composition	Toxic groups	Degradation products	Affected organ	Clinical symptoms	Generating fungi
1	2	3	4	5	6	7
Aflatoxins (B1, B2, G1, G2)	   	Difuran ring moiety's double-bonded lactic acid ring	AFB1 dihydrohydroxyl, AFB1-8,9-epoxide and AFB1-8,9-dihydrodiol	Immunity system, kidney, and liver	Hepatitis, abdominal pain, carcinogenic, vomiting, and immunosuppressive effects	<i>A. flavus</i> <i>A. nomius</i> <i>A. parasiticus</i>
Zearalenones (ZEA)	 	C-4 hydroxyl group on a lactone ring	1-(3,5-dihydroxyphenyl)-6'-hydroxy-1'-undecen-10'-one, α - β -zearalanol, α - β -zearalenol, zearalenone-4-sulfates, (5S)-5-(2,4-dihydroxy-6-(1E)-5-hydroxypent-1-en-1-yl] benzoyl]oxy) hexanoic acid	Reproductive system, mostly in females	Hyperestrogenism Reproductive disorders	<i>F. graminearum</i> <i>F. cerealis</i> <i>F. verticillioides</i> <i>F. culmorum</i> <i>F. equiseti</i> <i>F. roseum</i> <i>F. incarnatum</i>
Ochratoxins (A, B, C) (OTs)	  	Isocoumarin moiety Carboxyl group of the phenylalanine moiety Cl group	L- β -phenylalanine, OTa	Liver, kidney, immune system, inhibit RNA, DNA and protein synthesis in kidney	Nephritis, enlargement of kidney and hepatitis	<i>P. nordicum</i> <i>P. verrucosum</i> <i>A. ochraceus</i> <i>A. niger</i> <i>A. carbonarius</i>

Table 1 – contd.

1	2	3	4	5	6	7
Fumonisin FBs (B1, B2)		Free amino group, two side chains of tricarballic acid	2-oxo-12,16-dimethyl-3,5,10,14,15-icosanepentol hemiketal, N-acetyl API	Immunity system, liver, central nervous system (in horse), and heart and lungs (pig)	Equine leukoencephalomalacia and porcine pulmonary edema	<i>Fusarium</i> section <i>Liseola</i>
Trichothecenes (DON, T-2, HT-2) TCNs		Epoxide group Acylated side groups C9-10 double bonded	3 α ,7 α ,15 α - triacetoxycydeoxynivalenol, de-epoxy deoxynivalenol, HT-2 toxin, T-2 triol, T-2 tetraol, de-epoxy T-2 tetraol, diaacetoxycydeoxynivalenol, 3-acetyldeoxynivalenol, Epoxymonoacetoxycydeoxynivalenol, de-epoxycydeoxynivalenol	Digestive system, central nervous system, liver, and immunity system	Circulatory dysfunction, nausea, vomiting, anorexia, and abdominal pain	<i>F. acuminatum</i> <i>F. sporotrichioides</i> <i>F. langsethiae</i> <i>F. sporotrichioides</i> <i>F. graminearum</i> <i>F. cerealis</i> <i>F. culmorum</i> <i>F. culmorum</i> <i>F. poae</i>
Patulin PAT		Hemiacetal with a furan, pyran, or lactone ring	Ascladiol, hydroascladiol, desoxypatulinic acid, 3-keto-5-hydroxypentanal, glyoxylic acid	Liver, kidney, gut epithelium, and immune system	Appetite loss, oral epithelial lesions, vomiting, nausea and gastric ulcers	<i>A. clavatus</i> <i>Bysschlamis nivea</i> <i>Penicillium griseofulvum</i> <i>P. expansum</i>

Over 400 different varieties of mycotoxins have been discovered and documented since 1960. Mycotoxins that are very hazardous and frequently found in diets include aflatoxins, fumonisins, trichothecenes, patulin, ochratoxins, and zearalenone (ZEA) (Khan et al., 2020). A variety of toxic fungi may create these significant pollutants when inadvertently handled, stored, or transported (Marin et al., 2013). Most of them have intricate chemical compositions with distinct groups with hazardous effects. Basic facts regarding the major mycotoxins, including their chemical components, biological effects, and the fungus that produce them, are indicated in Table 1 (Gil-Serna et al., 2020; Khan et al., 2020). The four major types of aflatoxin are included in Figure 1.

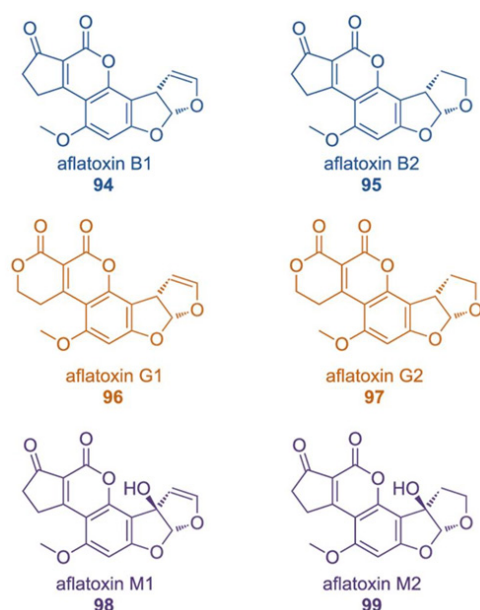


Figure 1. The four major types of aflatoxin

Mode of action of aflatoxin

Cytochrome P450 enzymes convert aflatoxin into the reactive 8,9-epoxide form, which is important for toxicity (phase I metabolism). However, CYP2A6 and, to a minor extent, CYP1A1 orthologs are the corresponding enzymes in turkeys and chickens (Diaz et al., 2010). DNA and proteins bind to the guanine residues of nucleic acids to form the epoxide metabolite that is cytotoxic and genotoxic (Doi et al., 2002). Hepatocellular carcinomas are caused by guaninecytosine (GC) to thymine-adenine (TA) transversions caused by the aflatoxin B1-DNA adducts (Jw, 2003), which results in irreversible DNA damage. Epoxide hydrolase and the hazardous epoxide metabolite were both detoxified by glutathione conjugation or hydrolysis to produce AFB1-8,9-dihydrodiol (AFB1-dhd) and phase II metabolism, respectively. AFB1 transformation into less harmful substances like aflatoxin Q1 (AFQ1) or (AFM1) (Diaz et al., 2010). The carcinogenic potential of the AFM1 metabolite is ten times lower than that of AFB1. These metabolites are found in the milk of cows. Humans are allowed to consume the highest milk concentrations of 0.05 g/kg, 20.0 ppb in grains,

and 4.0 ppb in agricultural products and foods (Enan et al., 2022). Depending on bacteria strain, concentrations, and pH conditions, probiotic bacteria have varying potentials for reducing aflatoxin. The pathways of aflatoxin disease in humans are illustrated in Figure 2.

Immunosuppression

Aflatoxin decreases the main and secondary innate immunity, which has an immunosuppressive impact on NK cell function and both cellular and humoral immunological function (Methenitou et al., 2001). AFB1 also causes thymic aplasia, which impairs T-lymphocyte function, lymphokines, and inhibits complement and phagocytic activities (Bondy and Pestka, 2000; Kataria et al., 2005). Proinflammatory cytokines, IFN, mRNA, tumor necrosis factor (TNF) alpha, as well as interleukin IL-1, -2, -6, are all decreased by aflatoxin (Marin et al., 2002).

Embryonic chickens exposed to AFB1 had suppressed graft-versus-host responses, thymic bursal involution, decreased cutaneous hypersensitivity, impaired macrophage activity, and lower antibody titers to the Marek's, Newcastle, and infectious bursal disease vaccines (Verma et al., 2004). Also, many mycotoxins damage immune-related tissues and cells, impacting the host's defense against infectious diseases and other microbial toxins (Kimura et al., 2004). Aflatoxins reduce the role of immunological processes, mainly cell-mediated immune response (Mohamed et al., 2022). For instance, in people with human immunodeficiency virus positivity, high amounts of AFB1-albumin adducts alter T-cell morphologies and decrease the proportion of B cells (Jiang et al., 2008). Besides affecting lymphocytes, embryonic exposure to AFB1 lowers the phagocytic potential, inhibits antiviral activity, and reduces chemotactic responses in phagocytes including macrophages and neutrophils (Cusumano et al., 1996). AFB1 also suppresses TNF, IL-1, and IL-6, which disrupts pulmonary and systemic host defenses by impairing macrophages' innate immunity (Bondy and Pestka, 2000).

Detoxification

Several approaches have been published to eliminate mycotoxin, as indicated in Figure 3. They may be loosely divided into physical (Bočarov-Stančić et al., 2011), chemical, and biological methods (Li et al., 2020). Although certain chemical and physical procedures can eliminate mycotoxin with varied degrees of effectiveness, several barriers, such as possible safety matters, loss of key nutrients, and expensive pricing, still hinder their utilization in the feeding industries (Huang et al., 2018). Recently, several biological detoxification methods, especially those utilizing microbial cells or enzymes, have been reported to be highly efficient at specifically converting mycotoxins into less harmful byproducts (Taheur et al., 2019; Afsah-Hejri et al., 2020).

Detoxification processes that are carried out by microbes or enzymes might occur in mild working circumstances with less damage to the nutritional value of food

items than chemical and physical treatments (Zhu et al., 2017; Lyagin and Efremenko, 2019). To date, various known bacteria and yeasts can decompose mycotoxins (Liuzzi et al., 2017; Rajasekharan et al., 2018). The direct extraction and purification of mycotoxins-degrading enzymes from biomaterials and their production in the mature microbial host through genetic engineering techniques have been widely described (Liu et al., 2018). Although the byproducts of detoxification can be more toxic than the original toxin, there have only been a few studies to evaluate their possible safety (Al-Nussairawi et al., 2020).

Due to issues with inadequate detoxification, financial implications, and equipment availability, constraints apply to the detoxification of agricultural products employing radiation, oxidation, ammoniation, alkalization, reduction, deamination, and acidification. Incorporating a mycotoxin detoxifying agent (also known as a mycotoxin detoxifier) into feed to minimize the toxin's bioavailability is a typical technique for reducing mycotoxin exposure in the field (Kolosova and Stroka, 2011). Detoxifiers

are frequently applied as feed supplements to avoid mycotoxin contamination of feed; mycotoxin modifiers and binders are two distinct kinds of detoxifiers. Mycotoxin binders absorb the toxin in the gut, causing a toxin-binder complex to be excreted in the stool, whereas mycotoxin modifiers convert the poison into non-toxic metabolites (Boudergue, 2009). Detoxifier does not imply that animal feed exceeds the highest permissible regulatory limits. Detoxifiers can be added to feed to increase its quality, making it more marketable and safe for animals' health (Kolosova and Stroka, 2011). However, despite the fact that the employment of microorganisms is predicted to be safe for both animal health and the production of harmless poultry products, there are still several microbes that cannot be directly incorporated in feed or food. Testing, screening, and selection of strains that have shown their efficiency in reducing or even suppressing aflatoxin B1 toxicity and being universally accepted as safe have been the main objectives of research to locate microorganisms for aflatoxin B1 management in recent years (Gao et al., 2011; Galarza-Seeber et al., 2015).

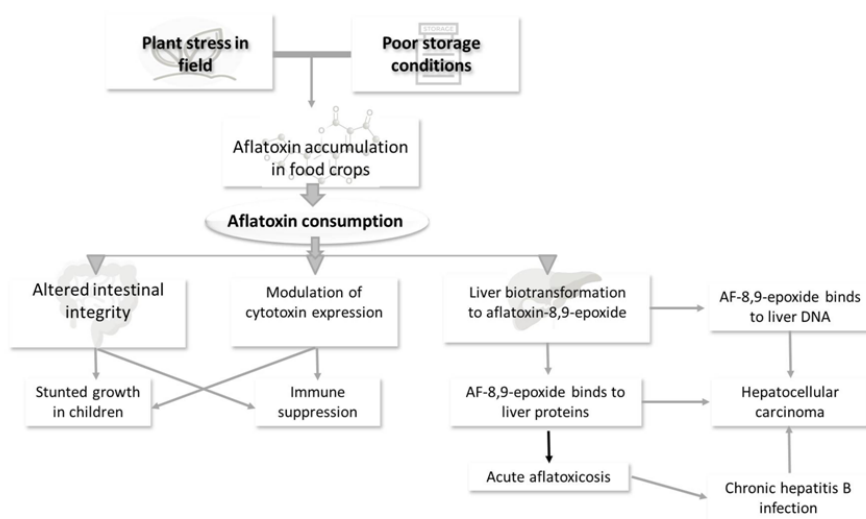


Figure 2. The pathways of aflatoxin disease in humans

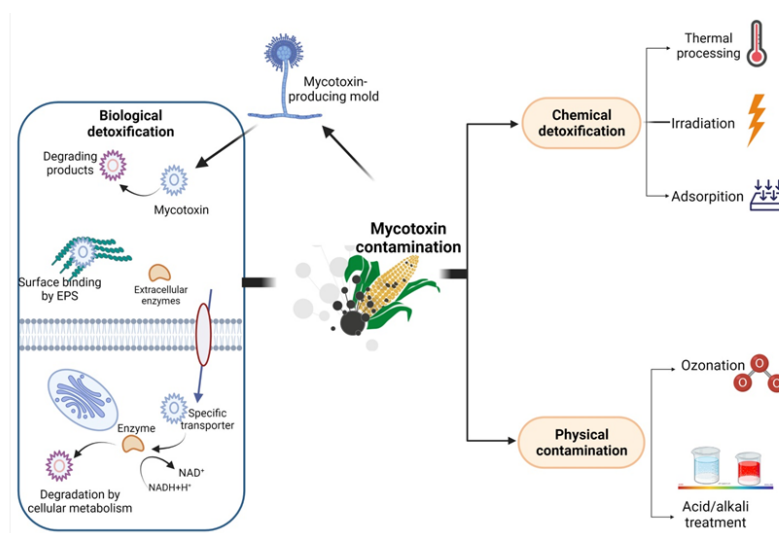


Figure 3. Schematic representation of mycotoxin detoxification methods

Similarly, Zolfaghari et al. (2020) reported that probiotic strains are the best biological solution to diminish AFB1 in the human gastrointestinal system. AFB1 can damage people. However, probiotic bacteria can aid in improving food safety. Probiotics (AVI-5-BAC) + ajowan may be introduced to the rabbit diet to lessen and detoxify, remove the toxicity of AFB1 and improve growth performance criterion. The strains of *Candida krusei*, *S. cerevisiae*, *L. fermentum*, and *L. plantarum* produced the best results (Shetty and Jespersen, 2006) when it was determined which lactic acid bacteria and yeast species have the capability of binding to AFB1. These strains reduced the amount of AFB1 in the saline by at least 60%. According to Peltonen et al. (2001), *L. rhamnosus* and *L. amylovorus* are highly efficient strains of binding 50% of AFB1 from a buffered saline solution, while *L. lactis*, *L. cremoris*, *Bifidobacterium lactis*, and *B. animalis* have a relatively lesser efficiency with 40 to 50%. Additionally, Kusumaningtyas et al. (2006) researched the decontamination of chicken diets containing AFB1 by employing *S. cerevisiae* and/or *Rhizopus oligosporus*. The concentration of AFB1 is reduced in both solo and combined treatments, with the greatest drop (about 60% reduction) occurring after five days of treatment. Nevertheless, probiotics can enhance feed utilization by synthesizing specialized hydrolytic enzymes interrupting carbohydrates and activating other enzymes including saccharase, maltase, and galactosidases (Štyriak et al., 2001).

Table 2 gives an overview of the mycotoxins breakdown by probiotics over the previous ten years. Where Harkai et al. (2016) chose several *Streptomyces* strains

that have demonstrated a good ability to digest the mycotoxins AFB1 and ZON with no genotoxicity. Rao et al. (2017) extracted CFR1 from *Bacillus licheniformis*, well-known bacteria that could digest aflatoxin B1 at a reduced rate of 94.7% in liquid culture conditions. Three *P. pentosaceus* strains were used to treat wheat grains by Juodeikiene et al. (2018), and a reduction of mycotoxins was found (deoxynivalenol (DON), T-2 toxin (T-2), and HT-2 toxin (HT-2)) in wheat grains (malts). Also, the yeast *S. pastorianus* A15 may inhibit the enzyme activities and toxicity of *Fusarium trichothecenes* in the brewer's wort fermentations, according to a study by Nathanail et al. (2016). The lowered rates were 15%, 17%, 34% and 31% for DON, DON3Glc, HT-2, and T-2, respectively. This strain can make a great choice for controlling mycotoxicosis during feed preparation.

According to Zhang et al. (2019), extracellular proteins or enzymes with a varied reaction temperature range of 20 to 70°C and a pH range of 5 to 9 are mostly responsible for the degradation. This information will be useful for their use in difficult circumstances while preparing food and feed. Several aflatoxin pathway genes, as well as two transcription factors (aflR and aflS) in A, may be down-regulated by *Bacillus amyloliquefaciens* WF2020, which can also suppress fungal growth and produce less AFB1. The enzymes or proteins found in the supernatant of this organism are brand-new, promising agents that can protect feed and food from AFB1 infection. *Bacillus amyloliquefaciens* WF2020 may be employed to take advantage of potential food and feed processing agents to lessen AFB1 contamination.

Table 2. Mycotoxin degradation by probiotic bacterial species

Mycotoxins	Bacterial strain	Reduction %	Toxicity level	Condition of degradation	References
AFB1	<i>Streptomyces cacaioi</i> subsp.	88.34±15.62	1 µg/ mL	LB liquid medium, 5 days, 170 rpm, and 28°C.	Harkai et al., 2016
	<i>asoensis</i> K234	79.930	1 µg/ mL		
	<i>S. luteogriseus</i> K144	94.73±1.090	500.0 ppb	liquid nutrient broth (Jiang et al., 2008) at 37°C, 72 h.	Rao et al., 2017
	<i>B. licheniformis</i> CFR1				
T-2	<i>P. pentosaceus</i> KTU05-10	78.0	12.8–19.5 µg kg ⁻¹	30 minutes of malting wheat grains in a bacterial solution at 18 °C	Juodeikiene et al., 2018
	<i>Saccharomyces pastorianus</i> A15	31.0	5000 µg/ L	Plato wort at 11.5°C, 120 rpm, for four days.	Nathanail et al., 2016
DON	<i>P. pentosaceus</i> KTU05-10	47.0	3370–930 µg kg ⁻¹	Malting wheat grains for 30 min in bacterial broth at 18°C	Juodeikiene et al., 2018
	<i>S. pastorianus</i> A15	15.0	400.0 µg/L	Plato wort, 120 rpm at 15°C for 96 h.	Nathanail et al., 2016
ZEA	<i>P. acidilactici</i>	38.0	19.5–73.7 µg L ⁻¹	30 minutes at 18°C while malting wheat grains with a liquid bacterial solution.	Juodeikiene et al., 2018
	<i>Streptomyces rimosus</i> (K145, K189)	100.0	1 µg mL ⁻¹	LB media, 170 rpm at 28°C for five days.	Harkai et al., 2016
HT-2	<i>P. pentosaceus</i> KTU05-10	79.00	258–819 µg/L	Bacterial suspension in wheat grains during a 30-minute malting process at 18°C	Juodeikiene et al., 2018

Health advantages of probiotic usage in aflatoxin management

Biological detoxification is an innovative and powerful method for removing mycotoxins from concentrated feed, raw materials, and food. Probiotic consumption has positive effects on the host organism that goes beyond simple common nutrition and has a tremendous ability to lower the bio-availability of ingested AFs. It seems that the particular strain, the food matrix, the dose, the manner, and the time of administration (continuous or cyclical) are crucial for achieving the desired health benefit. Since probiotic bacteria have positive impacts on human health, they are often used to make fermented foods. They can stop mold development and mycotoxins formation (Jard et al., 2011). The incorporation of probiotics in the feed and food business to reduce aflatoxin residues in eggs, milk, and meats was also mentioned (Ibrahim, 2022). Probiotics may thus be effective tools for reducing the harm that aflatoxin in the chicken business does to the economy and public health. Likewise, Chowdhury et al. (2020) revealed that dietary probiotics might increase laying performances and egg quality in terms of shell and albumen quality. Utilizing probiotics helps to enhance the biochemical blood markers of total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol.

According to Zolfaghari et al. (2020), using probiotic strains is the proper biological strategy to decrease AFB1 in the human gastrointestinal system. AFB1 can damage people. However, probiotic bacteria can aid in improving food safety. The robust colonization and adhesion of probiotics in the human gut, which boosts the human immune response, is necessary for them to function effectively in the same setting. As a result, studies utilizing *in vivo* techniques have been published on AFB1 and OTA in the digestive system in the presence and absence of probiotics (Elsanhoty et al., 2014). The average bioavailability of AFB1 was 90% without probiotics, but it decreased to 37% upon using six probiotic bacteria. Thus, the ability of the bacterial strains to attach to AFB1 varies (Gratz et al., 2006).

Additionally, the probiotic bacterial strains of *Propionibacterium* sp. and *Lactobacillus* sp. were used to reduce AFB1 in chicken duodenum by 57–66% (Doron and Gorbach, 2006). Aflatoxin B1 was decreased by 25–61% when *L. fermentum*, *L. easei*, and *L. plantarum* were grown in a liquid medium. Accordingly, Abdelmotilib et al. (2018) studied how aflatoxin M1 could be removed from milk using probiotic yeast and bacterial spp., including *S. cerevisiae*, *Bifidobacterium bifidum*, *L. acidophilus*, *L. plantarum*, and *Kluyveromyces lactis*, showing that the maximum levels of removing AFM1 were 90.88% followed by 88.60%, 86.64%, and 80.56% for the treated milk (Elsanhoty et al., 2014).

The probiotic bacteria's ability to connect varies for several causes. It is also noteworthy that the combined ability of the four strains to remove toxins was lower than the sum of each strain's abilities. It was also investigated whether lactic acid bacteria and bifidobacteria could re-

move mycotoxins other than AFB1. The ability of AFB1 to remove mycotoxin from the supernatant varied based on the strain (decrease in the supernatant ranged between 2.0 to 82.0%) and the strain-mycotoxin under discussion, but less so on the levels of PAT or OTA. For example, although *B. animalis* LA17 lowered less than 12% of both toxins, *B. animalis* VM12 decreased 22% of OTA and 82% of PAT. On the other hand, some bacterial species of *B. longum*, *L. plantarum*, and *L. acidophilus*, significantly lowered the OTA compared to PAT. According to Hernandez-Mendoza et al. (2009), eight isolates of *L. casei* were evaluated, and the removal capacity ranged from 14 to 50%, demonstrating strain-specific binding of AFB1 (Fazeli et al., 2009).

According to Orsi et al. (2007), aflatoxin's impacts on protein biosynthesis and cellular viability in the liver may result in lower protein content and albumin levels, and increased ALT activity may result from increased cell membrane permeability or hepatic necrosis. Furthermore, Marai and Asker (2008) hypothesized that aflatoxin's negative effects on immunity could reduce globulin levels. As a result, probiotics enhanced blood parameters, renal performance, and liver functions while reducing the impact of AFs on body weight increase, as demonstrated by El-Afifi et al. (2013).

Conclusion

Probiotics and/or prebiotics could be used in the food and feeding industry to reduce aflatoxin residues in meats, eggs, and even milk. Therefore, probiotics and prebiotics may be effective instruments for reducing the harm that aflatoxin does to the chicken industry's economy and public health. By raising awareness of the existence of aflatoxins in chicken products and the possible impact on animal and human health, public health should pay closer attention to food safety along the value chain.

Conflict of interest

All authors declare that they have no conflicts of interest that could inappropriately influence this manuscript.

Author contribution

All authors contributed equally to writing this review article. All authors read and approved the final version of this manuscript.

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