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Biological detoxification of mycotoxins by binding them with certain microorganisms: A review

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Abstract

Mycotoxins are harmful toxic metabolites of fungi that are present as contaminants in many foods, dairy, and agricultural products and constitute a potential health hazard. Therefore, novel decontamination approaches for decreasing its bioavailability are of huge interest to improve human safety. In recent years, biological methods have been developed to control mycotoxin contamination. The degradation of mycotoxins (especially aflatoxins (AFs), which are created by the genus Aspergilla species, mainly *A. parasiticus*, *A. flavus*, and *A. nomius*) using microorganisms is an important bio-based method to reduce mycotoxin levels in foodstuffs without the production of harmful intermediates and by-products. Many studies have reported that detoxification occurs by binding the mycotoxin to the cell wall structure of microorganisms. Several factors, including the microorganism strain, the type of toxin, microorganism concentration, the viability of the microorganism, and the contact period, are involved in the detoxification processes. This review discusses the available literature on the biological decontamination of mycotoxins by probiotic microorganisms (mainly), describes the detoxification mechanisms involved in such processes, and the factors influencing the stability of interactions. Future perspectives on this area are also reported. Based on the current data, one should be able to select the most efficient microorganisms to degrade mycotoxins over a wide range of concentrations.

1. Introduction

Mycotoxins are one of the most significant classes of naturally occurring toxins in many food, agricultural, and dairy products that can lead to considerable health risks. These potent toxic compounds are secondary metabolites formed during the growth of certain filamentous fungi, including *Aspergillus*, *Fusarium*, and *Penicillium* genera. These fungi play an undeniable role in food hygiene by producing toxic metabolites called aflatoxins (AFs) that are created by the genus *Aspergilla* species, especially *A. parasiticus*, *A. flavus*, and *A. nomius*, which grow on various raw materials. The adverse effect of AFs on human and animal health is called aflatoxicosis (Alassane-Kpembi et al., 2017). Among mycotoxins, Aflatoxin B1 (AFB1) is a well-known carcinogen that was added to the list of carcinogenic substances by the International Agency for Research on Cancer (IARC, 1993). Therefore, novel decontamination approaches to reduce its availability are important to improve human security (Marshall et al., 2020; Piotrowska, 2021).

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Several traditional physical adsorption approaches and some chemical reactions have been suggested to reduce production, cease activity, or eliminate the bioavailability of AFs in food/feed (Alassane-Kpembi et al., 2017; Marshall et al., 2020). However, the need for expensive equipment and/or practical difficulties are major drawbacks to these detoxification processes. In addition, the undesirable effects of intermediates and by-products have not been entirely measured. Therefore, researchers are increasingly interested in finding a secure and effective method to decontaminate mycotoxins.

Numerous studies in the literature concentrate on the decontamination of mycotoxins using microorganisms. Several studies have used "non-probiotic microorganisms" such as *Enterococcus faecium* strains (Topcu et al. 2010), *Mycobacterium fluoranthenivorans*, and *Rh. Rythropolis* (Teniola et al. 2005) to decontaminate AFB1. However, many microorganisms or their metabolites can also adversely affect consumers' health. Enzymatic functions are reportedly involved in the decontamination of mycotoxins by these microorganisms. For example, *Flavobacterium aurantiacum* was examined for its ability to detoxify AFs from food products. The results of the AFB1 degradation ability of *Bacillus subtilis* BCC 42005 indicated that AFB1 biotransformed into less toxic products due to enzyme activity (laccase) (Watanakij et al., 2020). It was also shown that AFB1 was biotransformed to compounds with different structures (AFD3, AFD2, AFD1) by *P. putida* via a modified lactone ring and furan on the AFB1 molecule (Samuel et al., 2014). Nakazato et al. (1990) studied the bio-transformations of AFB1 into aflatoxicol A, aflatoxicol B, and aflatoxin B_{2a} by *Rhizopus oryzae* and *Rh. oligosporus*. They found that the new ingredients produced by these conversions are less toxic than AFB1, but the safety of these new molecules is uncertain.

Recently, Ernuoa et al. (2020) and Qiu et al. (2021) studied the structural and toxicity of the by-products from the AFB1 biodegradation by culture supernatant of *Cladosporium uredinicola* and *Aspergillus niger* FS10. They concluded that the toxicity of biodegraded products (AFB2-GOH) was reduced compared with that of AFB1, and the double bonds of AFB1 had a high probability of being destroyed. Also, Zhang et al. (2020) reported enzymatic modification of deoxynivalenol (DON) by *Pelagibacterium halotolerans* ANSP101, which was capable of transforming DON to 3-keto-deoxynivalenol (with lower toxicity) through the oxidation of the C3 hydroxyl group. This study showed that the stirring activity of *Pelagibacterium halotolerans* was predominantly related to the bacterial cell lysate. In another study, *Bacillus velezensis* DY3108 showed the same ability for AFB1 biotransformation but into less cytotoxic products (Shu et al., 2018). Further examples include the *Cupriavidus* genus. (Al-Nussairawi et al., 2020), *Escherichia coli* CG1061 (Wang et al., 2019), and *Streptomyces* spp. (Campos-Avelar et al., 2021).

The toxicity of enzymatic and chemical degradation products and the adverse effects of non-probiotic microorganisms on food quality are controversial issues. Therefore, it is important to select a microorganism that efficiently binds AFs in a way that its inclusion in the food does not compromise human health. Several strains of LAB and some strains of *Saccharomyces cerevisiae* (SC) have probiotic activity and show potential as a tool to reduce mycotoxins by adsorbtion (Piotrowska, 2021; Taheur et al., 2017, 2020) or eliminate them (Ejiofor et al., 2021; Piotrowska, 2021). These microorganisms can bind to cell wall components of AFs in liquid media. Moreover, this biological detoxification is not only rapid and cost-effective but can also inhibit mould growth. As a result, the specific processes (formation of the microorganism–mycotoxin complex and the inactivation of mycotoxins) have been applied in the reduction and elimination of mycotoxins by microorganisms. In this review, the ability of microorganisms to control mycotoxins as a biological decontamination method via binding of mycotoxins to the cell wall of microorganisms as well as the factors involved in their interactions, are summarized.

2. Preventing mycotoxin production by inhibiting the growth of toxin-producing microorganisms

Preventing mycotoxin biosynthesis by inhibiting toxicogenic mould growth is the preferred method to control the presence of mycotoxins in foodstuffs (Pandey et al. 2016). Most data related to the bio-preservative function of bacteria, especially lactic acid bacteria (LAB), focus on their anti-bacterial effects. The abilities of the *Lactobacillus* genus to inhibit *A. parasiticus* and *A. flavus* growth have been reported in several studies. Previous studies have shown that during cell lysis, *L. casei* releases molecules that exclude *A. flavus* growth (Gourama & Bullerman, 1995).

Wiseman and Marth (1981) reported the relationship status between *A. parasiticus* and *Streptococcus lactis* and the reduction of AFs production. These results agree with those of others who found a significant reduction of *A. flavus* and *A. parasiticus* growth by *St. lactis* (Roy et al., 1996). Afsah-Hejri (2013) reported the biocontrol activities of saprophytic yeasts (*Cryptococcus albidus*, *C. hungaricus*, *Pseudozyma fusiformata*, *Rh. Hinula*, and *Rhodotorula fragaria*) isolated from pistachio fruits and leaves against *A. flavus.* This study showed that *Pseudozyma fusiformata* was the most effective for reducing spores. Moreover, Ismaiel et al. (2011) showed that kefir grains, kefir suspensions, and kefiran, which contain probiotic microflora, have antimicrobial activities versus the growth of *A. flavus* AH3 and therefore repress AF production. Zhu et al. (2017) summarized methodologies and strategies in each stage of the growth of microbiological solutions for the decontamination of mycotoxins in feed or food.

Campos-Avelar et al. (2021) recently reported the relationship between *Aspergillus flavus* growth inhibition and AFB1 detoxification by *Streptomyces* isolates. Shang et al. (2019) reported the ability of *the Bacillus megaterium s*train as a potential biological agent for controlling the toxigenic fungal growth of *Aspergillus ochraceus* and the elimination of ochratoxin A (OTA).

According to the above studies, using molds and yeasts with the ability of biological preservation is an acceptable method for preventing the growth of mycotoxin-producing microorganisms and thus stopping the production of toxins. However, it should be noted that the main problem of food/feed is the presence of poison in the final product. Therefore, we need to look for safe mechanisms that reduce/eliminate toxins.

3. The mechanism of binding mycotoxins to yeast and bacteria

Basic differences in the structure of yeast and bacteria are responsible for their various abilities to bind mycotoxins. The cell wall of yeast consists mostly of β-glucan and mannan oligosaccharides (Shetty & Jespersen, 2006). β-glucans are chains of glucose molecules joined by β-1,3 and 1,6 linkages. Mannan oligosaccharides comprise approximately 50% of the yeast carbohydrate value in the cell wall, and β-1,3 and 1,6-D-glucans are ingredients of the cell wall, which has a sufficiently high glucan content (30–60% dry weight) (NIA, 2005).

Based on some studies, the removal of mycotoxins by yeasts occurs via their adherence to the cell wall rather than via covalent binding (Baptista et al., 2004; Raju & Devegowda, 2000; Santin et al., 2003). However, in rats fed with mannan oligosaccharides and dried yeast, mannan oligosaccharides did not significantly repress the aflatoxin-induced damages (Baptista et al., 2004). A subsequent study confirmed the cell walls protective effects of *Candida utilis* ATCC 9950 and (1,3)/(1,6)-glucan as a trap adsorbing zearalenone (ZEN), AFB1, and OTA (Bzducha-Wróbel et al., 2019).

In an *in vitro* study with a *Saccharomyces cerevisiae* cell wall component, a dose-dependent binding of up to 77% (w/w) occurred, and modified mannan-oligosaccharides derived from the media resulted in up to 95% (w/w) binding

(Devegowda et al., 1996). This finding indicates that a cell wall containing mannan components play a major role in AF binding by SC. Esterified glucomannan, a cell wall derivative of SC, was shown to bind significant quantities of AFB1 and two other toxins (OTA and T-2 toxin) (Raju & Devegowda, 2000). Yiannikouris et al. (2004 a, 2004b) reported the binding of ZEN to β-D-glucans. A different study showed that β-1,3-glucan could strongly bind to T-2 toxin and ZEA in modified yeast (Freimund et al., 2003). When yeast cells are replaced with cell wall extract, the binding of ochratoxin A (OTA) is also elevated (Huwig et al., 2001). Furthermore, very rapid detoxification from a liquid medium indicated that the binding of OTA has a physical basis (Bejaoui et al., 2004). Yiannikouris et al. (2004c) reported basic interactions between β-D glucans and ZEN using X-ray and NMR diffraction studies. They showed that the chains of β-1,3 D-glucan are a very stable intra-helical connection with ZEN, which is fixed by β-1,6 D-glucan side chains. The sites of van der Waals and hydrogen bond interactions were recognized within the component and could thus be used as a basis to monitor the aggregation between the two molecules. Therefore, based on these findings, carbohydrates seem to have common sites for binding to toxins (Yiannikouris et al., 2004c). However, further studies with physic-chemically and live-modified intact yeast cells are needed to recognize the role of cell wall ingredients in mycotoxin binding. For example, the role of *Candida utilis* ATCC 9950 cell walls consisting mostly of β(1,3)/(1,6)-glucan in the adsorption of mycotoxins, including AFB1, OTA, DON, zearalenone (ZEN), nivalenol (NIV), T-2 toxin, and fumonisin B1 (FB1), as reported by Bzducha-Wróbel et al. (2019).

The cell-wall structures of gram-positive bacteria consist of a peptidoglycan matrix that forms the major cell-wall structural component and other components, including a proteinaceous S layer, teichoic and lipoteichoic acid, and neutral polysaccharides (Shetty & Jespersen, 2006). Bacterial cell wall components have different functions, including macromolecular binding and adhesion, especially to the fibrillar network of neutral polysaccharides and teichoic acids. A schematic view of the adsorption of AFs by microorganisms is given in Figure 2. Peptidoglycan or phosphoric acid in the cytoderm of microorganisms can absorb AFs through hydrophobic and electrostatic interactions (Guan et al., 2021).

Tentative evidence suggests that both polysaccharides and peptidoglycan play a role in the binding of toxins. Peptidoglycan or similar structures associated with peptidoglycan are involved in AFB1 binding (Lahtinen et al., 2004). Based on the study by Haskard et al. (2000), the mechanisms of AF binding to *Lb. rhamnosus* by applying enzyme treatments are related to cell wall protein and/or carbohydrate components. Pronase E, periodate treatment of acid and heat, and viable LAB strains resulted in a considerable decline in AFB1 binding. Haskard et al. (2000) also found that the binding of AFB1 was unaffected by pH (with ranges 2.5 - 8.5), presenting the lack of a cation exchange mechanism. Concerning the mechanism of activities involved in the detoxification of FB2 and FB1 by LAB, Niderkorn et al. (2006) stated that the most probable places for fumonisins binding are "peptidoglycans". This study also attributed the elimination of fumonisins by LABs to adhesion to cell wall components rather than to metabolism or covalent binding since defunct cells fully sustained their binding ability.

A mathematical model was reported by Bueno et al. (2007) to explain the *in vitro* removal of AFB1 by LAB and SC. This model brings up that the binding of the toxin onto the surface of the microorganisms and its release follow a reversible process. These findings confirm the reports of El-Nezami et al. (1998) that detoxification is dependent on the number of cells and that an increase in the number of bacteria can only be effective in removing up to 90% of the toxin. A schematic view of the biological mechanism of mycotoxin detoxification is given in (Figure 1).

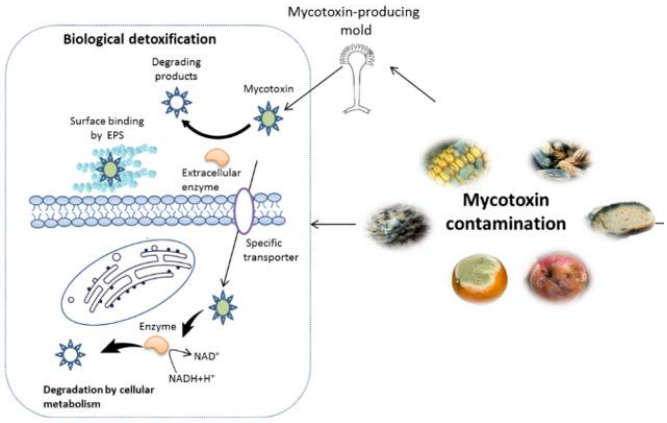

Figure 1. Schematic representation of the main mechanism of biological detoxification of mycotoxins: surface binding by extracellular polymeric substances (EPS), degradation by enzymes, and cellular metabolism (Adapted from Liu et al., 2022).

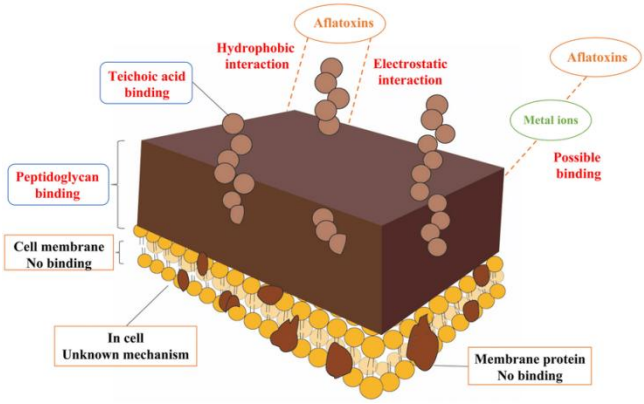

Figure 2. The adsorption of AFs by microorganisms (i.e., AFB1). Microorganisms can adsorb AFs through peptidoglycan or phosphoric acid in the cytoderm and hydrophobic and electrostatic interaction (Adapted from Guan et al., 2021).

4. Microorganism–mycotoxin interaction via binding processes

The cell-wall surface of microorganisms binds various molecules such as dietary carcinogens and toxins, metal ions, and mutagenic compounds. Studies related to the interaction of yeast and/or bacteria with AFs go back to the 1970s (Mann, 1977). (Table 1) lists such studies concerning mycotoxin reduction by yeasts. Santos et al. (2000) showed that the toxin from a yeast isolated from fermenting olive brines, called *Pichia membranifaciens* CYC 1106, binds primarily to the (1→6)-β-d-glucan of the cell wall of a sensitive yeast (*Candida boidinii* IGC 3430). Other studies have found that the SC strains RC016, RC08, and CECT 1891 were the best detoxifying microorganisms since they showed great efficiency for AFB1 exclusion (Ejiofor et al., 2021; Pizzolitto et al., 2011). The SC cell walls obtained from breweries as feed additives in the diet of poultry (Santin et al., 2003) and beer fermentation residue containing SC (Campagnolo et al., 2015) were reported to possess AFB1-binding capacity. The results of previous investigations also showed that some strains of both viable and non-viable SC effectively bind AFs (Bueno et al., 2007; Shetty et al., 2007). SC has revealed a potent adsorbent capacity and improved weight gain in rats fed with AFB1contaminated corn (Madrigal-Santillán et al., 2006).

Similar results were obtained with other microorganisms, such as *Lb. plantrium* in dairy products (Elsanhoty et al., 2014) and SC with several LABs (Corassin et al., 2013), which can bind aflatoxin M1 (AFM1). In another study, a mixture of yeast and beer fermentation residue was shown to efficiently bind OTA (Grunkemeier, 1990). This binding was depended on pH (maximum at pH 3.0) suggesting that the physical binding to cell walls might remove or eliminate OTA. Bejaouii et al. (2004) suggested that certain strains of SC can be used for the detoxification of OTA in natural and synthetic grape juice. In this regard, Markowiak et al. (2019) investigated the ability of probiotic strains of LAB and SC, from three different synbiotic for poultry, to detoxify OTA. Cell wall from SC has also been shown to bind remarkable amounts of ZEN, a well-known mycotoxin, where β-D glucans are the principal components involved in the establishment of the complex (Yiannikouris et al., 2004a, 2004b).

Several studies have reported mycotoxin reduction by certain bacteria (Table 2). Strains of LAB not only inhibit AF biosynthesis but also remove AF from contaminated products. Microorganisms from the genera Lactobacillus,

Bifidobacterium, Propionibacterium, and Lactococcus have been active in removing AFB1 primarily by a binding mechanism (Gratz et al., 2005; Haskard et al., 2001; Khanafari et al., 2007; Peltonen et al., 2001). Several LABs were reportedly able to bind with AFB1 *in vivo* and *in vitro* (Gratz et al., 2004), with the yield depending on the bacterial strain and its concentration. El-Nezami et al. (1998) measured the ability of dairy strains of LAB to bind AFB1 in liquid media and showed probiotic bacteria such as *Lb. rhamnosus* strains GG and LC-705 were very effective in removing AFB1. Similarly, Haskard et al. (2001) demonstrated that *Lb. rhamnosus* strains GG (ATCC 53103) and LC-705 (DSM 7061) eliminated AFB1 from the culture media by a surface-binding process (Haskard et al., 2001). *In vitro* studies have shown *Lb. plantrum* C88 isolated from Chinese traditional fermented foods is able to reduce the toxicity of AFB1 by a binding process (Huang et al., 2017). Peltonen et al. (2001) found that *Lb. rhamnosus* and *Lb. amylovorus* can bind more than 50% of the available AFB1. Other studies have shown that *Lb. rhamnosus* strain GG can bind AFB1 and increase the maintenance of AFM1 and AFB1 metabolite within the gastrointestinal (GI) tract (Gratz et al., 2006) and reduce AFB1 transport, metabolism, and toxicity (Gratz et al., 2007). In other studies, the bacterial strain *Lb. casei* were bound to AFB1 (Hernandez-Mendoza et al., 2009).

Relevant results from other mycotoxins, including OTA. *Lb. acidophilus* VM 20, reduced OTA up to 95% (Fuchs et al. 2008). The strains of SC var. *boulardii* ATCC MYA-796 and SC (W13, W28, BM45) removed OTA by up to 44% (Petruzzi et al., 2016). Niderkorn et al. (2009) demonstrated the susceptibility of *Streptococcus thermophilus* RAR1 and *Lb. paraplantarum* CNRZ 1885 to bind fumonisins B1 and B2 (FB1 and FB2, respectively) in the GI tract and fermented food and feed, these bacteria contributed to the reduction in the bioavailability and toxic effects of FB1 and FB2 in farm animals and humans. In a recent study, *Lb. bulgaricus* was shown to be effective in reducing the free AFM1 rate in a liquid culture medium (El Khoury et al., 2011).

Table 1. Examples of reported studies on mycotoxin decontamination by yeasts based on binding mechanism**.**

Mycotoxin	Microorganism (Yeast)	Source
AFB1	*S. cerevisiae*	Bueno et al. (2007) Campagnollo et al. (2015) Devegowda et al. (1996) Ejiofor et al. (2021) Madrigal-Santillán et al. (2006) Pizzolitto et al. (2011) Pizzolitto et al. (2012) Rahaie et al. (2010) Raju & Devegowda (2000) Shetty et al. (2007)
AFB1	*Candida utilis* ATCC 9950	Bzducha-Wróbel et al. (2019)
AFB1	*Aspergillus niger*	Qiu et al. (2021)
AFM1	*S. cerevisiae*	Corassin et al. (2013)
FUB1	*S. cerevisiae*	Pizzolitto et al. (2012) Raju & Devegowda (2000)
OTA	*S. cerevisiae*	Bejaouii et al. (2004) Grunkemeier (1990) Markowiak et al. (2019) Raju and Devegowda (2000) Petruzzi et al. (2016)
OTA	*Candida utilis* ATCC 9950	Bzducha-Wróbel et al. (2019)
ZER	*S. cerevisiae*	Raju & Devegowda (2000) Yiannikouris et al. (2004a, 2004b)
ZER	*Candida utilis* ATCC 9950	Bzducha-Wróbel et al. (2019)
T-2 toxin	*S. cerevisiae*	Raju & Devegowda (2000)

Table 2. Examples of reported studies on mycotoxin decontamination by bacteria based on binding mechanism

Mycotoxin	Microorganism (Bacteria)	Source
AFB1	*Propionibacterium freudenreichii subsp. shermanii* JS	Lee et al. (2003)
AFB1	*Escherichia coli* CG1061	Wang et al. (2019)
AFB1	*Streptomyces* spp.	Campos-Avelar et al. (2021)
AFB1	Cupriavidus genus.	Al-Nussairawi et al. (2020)
AFB1	*Lb. rhamnosus* GG *Lb. rhamnosus* LC-705	Bueno et al. (2007) El-Nezami et al. (1998) Gratz et al. (2007) Haskard et al. (2001) Lee et al. (2003) Peltonen et al. (2001)
AFB1	*Lb. rhamnosus* C88	Huang et al. (2017)
AFB1	*Lb. amylovorus* CSCC 5197 *Lb. amylovorus* CSCC 5160	Peltonen et al. (2001)
AFB1	*Bifidobacterium animalis* *Bifidobacterium lactis*	Peltonen et al. (2001)
AFB1	*Enterococcus faecium* strains	Topcu et al. (2010)
AFB1	*Rhodococcus rhodochrous* NI2	Krifaton et al. (2011)
AFB1	*Nocardia corynebacterioides* DSM 12676 *Nocardia corynebacterioides* DSM 20151 *Rhodococcus erythropolis Mycobacterium fluoranthenivorans* sp. nov. DSM 44556^{T}	Teniola et al. (2005)
AFB1	*Gluconobacter oxydans*	Markov et al. (2019)
AFB1	*Lb. casei*	Hernandez-Mendoza et al. (2009)
AFM1	*Lb. bulgaricus* *Streptococcus thermophilus*	El-Khoury et al. (2011)
AFM1	*Lb. rhamnosus,* *Lb. delbrueckii spp. bulgaricus Bifidobacterium lactis*	Corassin et al. (2013)
AFM1	*Lb. Plantrium*	Elsanhoty et al. (2014)
FB1 and B2	*Lb. paraplantarum* CNRZ 1885 *Streptococcus thermophilus* RAR1	Niderkorn et al. (2009)
FB1 and B2	*Lb. rhamnosus* GG *Lb.plantarum* *Lb..brevis* *Lb.acidophilus* *Lb.delbruekii ssp. Bulgaricus* *Lb.reuteri* *Lb.buchneri* *Lb.helveticus* *Lb.lactis* *Lb.casei ssp. Casei* *Lactococcus lactis* *Leuconostoc mesenteroides*	Niderkorn et al. (2006)
FB1	*Lb. acidophilus*	Pizzolitto et al. (2012)
OTA	*Gluconobacter oxydans*	Markov et al. (2019)
ZEN	*Lb.plantarum*	Chen et al. (2018)

5. Factors involved in microorganism–mycotoxin interactions

The use of microorganisms for reducing mycotoxin availability depends on the stability of the complex formed in the GI tract. In the case of unstable binding interactions, mycotoxins can be released by the repeated washing of the bacterial surface in the GI tract (Pizzolitto et al., 2011). In several studies, the stability of the

microorganisms–mycotoxins complex was determined by continual washings of the cellular pellets previously bound to the mycotoxin with acetonitrile (an organic solvent suitable for dissolving AFB1) or phosphate-buffered saline (PBS, an aqueous solvent). Pizzolitto et al. (2011) reported ≥90 AFB1 release by organic solvent (acetonitrile) treatment and 50% release by PBS treatment after five washing cycles for both treatments. The washing time (from 1 to 60 min) did not impact the release percentage (Pizzolitto et al., 2011). These findings prove that the process is rapid and reversible and supports the idea that the cells are unable to metabolically convert the toxin because AFB1 was released from the microorganism with the same chemical composition as before. Pizzolitto et al. (2012) found a similar reversible process with *Lb. acidophilus* 24 and SC strain CECT 1891 to remove FB1 from the liquid medium. Researchers have reported the reversibility of the process. For example, Haskard et al. (2001) investigated LAB strains in viable and non-viable forms and showed the AFB1 binding was reversible after several consecutive washes. They concluded that AFs binding to the surface of the cell wall is extremely powerful, with *Lb. rhamnosus* strains LC105 and LGG cells in viable forms retained 50 and 38% (w/w) of the bound toxin, respectively, after several washes. However, non-viable cells treated by acid and heat kept toxins up to 71% (w/w), leading to a high stability of the formed complex. This situation described better accessibility for the molecular groups present in the treated cells. Moreover, the studies also showed that the type of washing solution used affects the release rate of the bound toxin (Haskard et al., 2001). Similar findings have been reported in other studies indicating 20–30% of bound AFB1 was released by PBS and proposed that bacteria adhered to the AFB1 with non-covalent, weak interactions that are partly reversible (Hernandez-Mendoza et al., 2009; Peltonen et al., 2001). Similarly, Petruzzi et al. (2016) reported that 18-28% of OTA exhibited reversible, not stable binding with the strains of SC.

The degree of microorganism adhesion to the intestine is a major factor in the treatment of toxins in the GI tract. Studies have shown that LABs are significantly more capable of adhering to intestinal cells than SC. However, adhesion rates for both LAB and SC appear to be highly specific and strain-dependent. Although some strains of microorganisms are rapidly eliminated from the GI tract, SC cells tolerate the harsh environment of the GI tract well. Lee et al. (2003) observed a linear relationship between the number of washes and the natural log value of the concentration of AFB1 adsorbed for all bacteria studied. In another study, Chen et al. (2018) reported that *Lactobacillus plantarum* is able to decontaminate the GI tract from animal feed contaminated with ZEN, but a high number of cells (for binding to ZEN) is needed to perform this connection, and also degradation time is limited.

Based on the results of previous studies, the strength of the interaction between mycotoxin and LAB is influenced by the shape of peptidoglycan and its amino acid composition (Niderkorn et al., 2009). With low pH conditions in the stomach, the survival of live bacteria is significantly reduced. In addition, the remarkable adhesion property of some LABs to intestinal cells is lost when they bind to mycotoxins such as AFB1 (Gratz et al., 2004). Consequently, the mycotoxin–bacteria complex in the GI tract is rapidly excreted. Furthermore, trial-feeding animals with yeast cell walls and whole yeast has shown that adding SC to their diet leads to a reduction in mycotoxin toxicity. This finding suggests that the yeast-mycotoxin complex is likely to be stable in the GI tract (Santin et al., 2003)

Many studies have focused on the conditions and factors involved in mycotoxin removal and the interaction between microorganisms and mycotoxins. The microorganism strain is one of the factors that determine the efficiency of the microorganism–mycotoxin complex. In some studies, LAB is considered to bind AFB1 inefficiently, which might be due to the low binding ability of the strains used. Fazeli et al.

(2009) reported that *Lb. casei* had great physical power binding ability to aflatoxin compared to other LAB strains such as *Lb. plantarum*. Considering the difference in the binding rate of aflatoxin to different LAB strains, it can be concluded that the binding ability depends specifically on the type of LAB strain. A similar study was conducted on the ability to remove fumonisins by propionic and lactic acid bacteria. The results showed that LAB strains were significantly more effective than propionic acid bacteria in mycotoxin removal, and the differentiations between strains were high. (Niderkorn et al., 2006). The results of the Bueno et al. (2007) investigation also showed that SC was the most efficient microorganism to bind to aflatoxin. These findings confirm the findings of Pizzolitto et al. (2011), which suggested that the strain type affects the efficiency of microorganisms. Apart from studies on yeasts and LAB to bind, biodegrade, or remove mycotoxins, in recent years, Markov et al. (2019) reported the potential ability of *Gluconobacter oxydans* for physical binding to bacterial cell wall proteins and polysaccharides or biotransformation of mycotoxins (OTA and AFB1). This strain is a gram-negative acetic acid bacteria used in the food industry because of its innocuousness to human safety.

The mycotoxin concentration is another critical factor in mycotoxin–microorganism interactions. The detoxification related to different concentrations of AFB1 by LAB and yeasts has been reported in several studies. Lee et al. (2003) suggested that AFB1 binding is a limitless process with a linear relationship with the toxin concentration. They concluded that the surface of bacteria does not have a defined number of binding sites. However, other studies did not confirm these conclusions. The results of Pizzolitto et al. (2011) suggested that saturation phenomena could not be observed in the study of Lee et al. (2003) due to the high number of microorganisms used in the experiment. Pizzolito et al. (2011) showed that increasing the concentration of yeast or bacteria increased the removal of AFB1 through increased binding but never removed all the toxins in the medium. They concluded that with increasing concentration of AFB1, the amount of toxin removed also increases, but eventually, the percentage of toxin removal decreases due to the saturation of the binding sites. Therefore, it can be concluded that microorganisms have a limited number of AFB1 binding sites, either occupied or free sites.

Contact time between microorganisms and mycotoxin is not a major factor for microorganism-mycotoxin interactions. Several studies have shown no significant differences in AFB1 elimination by LAB after 3h, 6h, and 72h incubation with the toxin (El-Nezami et al., 1998; Peltonen et al., 2001; Pizzolitto et al., 2011; Rahaie et al., 2010). Shetty et al. (2007) also observed no difference in the binding of AFB1 by SC between 0.5 and 12 h of contact, which agrees with the findings of Pizzolitto et al. (2011). The experimental outcomes of Bueno et al. (2007) with LAB and SC indicated that the binding of AFB1 to microorganisms was a rapid process (less than 1 min). The same results were obtained with other mycotoxins containing OTA, where 90% (w/w) of the toxin was bound during the first 5 min (Bejaouii et al., 2004). Therefore, it can be deduced that toxin binding is a quick process since the microorganism was able to bind an equal amount of mycotoxin within 1 min as in several hours. More studies related to the use of several microorganisms based on a binding mechanism and contact time are listed in (Table 3).

The viability of the microorganism is another crucial factor that affects the mycotoxin–microorganism interaction. Different studies have reported on the elimination of AFB1 by viable or non-viable cells (Table 4). El-Nezami et al. (1998), Huang et al. (2017), Lee et al. (2003), Niderkorn et al. (2006), Rahaie et al. (2010), and Shetty et al. (2007) showed that applying heat and acid treatment on microorganisms increases their binding ability between 20 and 90%. The quenching abilities of microorganisms were increased when bacteria or yeast was killed using different physical or chemical treatments. Otley et al. (2000) reported that since heat treatment of bacteria often removed AFB1 more effectively

than the viable cells, a metabolic degradation process cannot be responsible for AFB1 elimination. Similar results were published for other mycotoxins, including OTA. Bejaouii et al. (2004) showed that heat-treated SC cells have a higher capacity for binding than viable cells indicating that the physical nature of binding and that cell density plays a significant role in the adsorption output for removing OTA from grape juice. These findings show that acid and heat treatments cause protein denaturation and removal of more hydrophobic surfaces (Haskard et al., 2000). Furthermore, when an organic solvent was used to treat cells, extraction of the bound toxin was rapid, confirming the potential role of hydrophobic interactions in AFB1 binding (Haskard et al., 2000). However, these results differ from those of other reports for some tested strains (Bueno et al., 2007; Haskard et al.,(2001; Pizzolitto et al., 2011, 2012; Topcu et al., 2010) who reported no significant difference between viable and non-viable cells in toxin elimination. Pizzolitto et al. (2011) concluded that binding might occur on the cell wall, that the mechanism involved did not need metabolic conversion of the toxin by cells, and that the entire number of microorganisms (cells mL^{-1}) should be utilized to estimate the cellular concentration instead of CFU mL^{-1}.

Table 3. Examples of reported studies on the mycotoxin degradation ability of several microorganisms based on a binding mechanism and contact time.

Microflora	Mycotoxin	Degradation (%)	Time (h)	Source
Nocardia corynebacterioides DSM 12676	AFB1	60	24	Teniola et al. (2005)
Nocardia corynebacterioides DSM 20151	AFB1	> 90	24	Teniola et al. (2005)
Rhodococcus erythropolis	AFB1	> 90	4 and 8	Teniola et al. (2005)
Rhodococcus rhodochrous NI2	AFB1	> 90	–	Krifaton et al. (2011)
Mycobacterium fluoranthenivorans sp. nov. DSM 44556^T	AFB1	> 90	4 and 8	Teniola et al. (2005)
Enterococcus faecium M74	AFB1	19.3 to 30.5	48	Topcu et al. (2010)
Enterococcus faecium EF031	AFB1	23.4 to 37.5	48	Topcu et al. (2010)
Lb. casei L30	AFB1	49.2	–	Hernandez-Mendoza et al. (2009)
Bacillus subtilis BCC 42005	AFB1	50	2	Watanakij et al. (2020)
Lb. bulgaricus	AFM1	58.5	6	El-Khoury et al. (2011)
Streptococcus thermophilus	AFM1	37.7	6	El-Khoury et al. (2011)
Lb. rhamnosus, *Lb. delbrueckii spp. bulgaricus* *Bifidobacterium lactis*	AFM1	11.5± 2.3 11.7± 4.4	0.5 1	Corassin et al. (2013)
Lb. acidophilus VM 20	OTA	≥ 95	–	Fuchs et al. (2008)
Bacillus megaterium JSW-B1	OTA	80.3	72	Shang et al. (2019)
S. cerevisiae	OTA	31.9	24	Markowiak et al. (2019)
Lb. rhamnosus GG	AFB1	80	0	El-Nezami et al. (1998)
Lb. rhamnosus LC-705 (LC705)	AFB1	80	0	El-Nezami et al. (1998)
Lb. rhamnosus *Lb. amylovorus*	AFB1	> 50	72	Peltonen et al. (2001)
S. cerevisiae	AFM1	90.3± 0.3 92.7± 0.7	0.5 1	Corassin et al. (2013)
S. cerevisiae	AFB1	≥ 95	–	Devegowda et al. (1996) Shetty et al. (2007)
S. cerevisiae	AFB1	40and 70	2 and 3	Rahaie et al. (2010)
S. cerevisiae	OTA	90	0.08	Bejaouii et al. (2004)

Table 4. Influence of heat and acid treatment of microflora on mycotoxin degradation ability.

Microflora	Mycotoxin	Treatment		Degradation (%)	Source
		Heat	Acid		
S. cerevisiae	AFB1	120 °C for 20 min	–	>100%	Shetty et al. (2007)
S. cerevisiae	AFB1	–	2 M HCl	>100%	Shetty et al. (2007)
S. cerevisiae	AFB1	120 °C for 20 min	–	55%	Rahaie et al. (2010)
S. cerevisiae	AFB1	–	2 M HCl	60%	Rahaie et al. (2010)
Lb. rhamnosus	AFB1	120 °C for 20 min	–	90%	Rahaie et al. (2010)
Lb. rhamnosus	AFB1	–	2 M HCl	90%	Rahaie et al. (2010)
Lb. rhamnosus strain GG *Lb. rhamnosus strain* LC-705	AFB1	121 °C for 45 min	–		El-Nezami et al. (1998)
Lb. rhamnosus GG *Lb. rhamnosus* LC-705	AFB1	100 °C for 60 min			Lee et al. (2003)
Lb. rhamnosus GG *Lb.plantarum* *Lb..brevis* *Lb.acidophilus* *Lb.delbruekii ssp. Bulgaricus* *Lb.reuteri* *Lb.buchneri* *Lb.helveticus* *Lb.lactis* *Lb.casei ssp. Casei* *Lactococcus lactis* *Leuconostoc mesenteroides*	FB1 and B2	100 °C for 60 min	–	> 82% FB1 >100%FB2	Niderkorn (2006)
S. cerevisiae	OTA	100 °C for 60 min	–	75%	Bejaouii et al. (2004)
S. cerevisiae	OTA	–	2 M HCl	75%	Bejaouii et al. (2004)
Bifidobacteria bifidum BGN$	AFB1	95 °C for 30 min	–	46± 4%	Oatley et al. (2000)
S. cerevisiae *Lb.acidophilus* *Lb. rhamnosus* *Lb. fermentum* *Lb. animalis*	AFB1	121 °C for 20 min	–	ineffective	Bueno et al. (2007)
Enterococcus faecium M74 *Enterococcus faecium* EF031	AFB1	121 °C for 20 min	–	ineffective	Topcu et al. (2010)
Lb. rhamnosus GG *Lb. rhamnosus* LC 705	AFB1	100 °C for 60 min	2 M HCl	ineffective	Haskard et al. (2001)
Lb. fermentum 23 *Lb. acidophilus* 24 *Lb. casei subsp. rhamnosus* *Lb. rhamnosus I* *Lb. paracasei subsp. paracasei* *Lb. casei 1* *S. cerevisiae* CECT 1891 *S. cerevisiae* 08 *S. cerevisiae RC016*	AFB1	121 °C for 20 min	–	ineffective	Pizzolitto et al. (2011)
Bacillus velezensis DY3108	AFB1	80°C	–	94.70	Shu et al. (2018)
S. cerevisiae CECT 1891 *Lactobacillus acidophilus* 24	FB1 AFB1	121 °C for 20 min	–	ineffective	Pizzolitto et al. (2012)

6. Conclusion

Due to the potential presence of mycotoxins in food and feed, it is necessary to find a safe detoxification method to protect against the undesirable effects of toxic metabolites. Studies have shown that the inclusion of microorganisms in the diet can help remove mycotoxins by avoiding the absorption of toxins during their GI transit. In a previous literature review, Vanhoutte et al. (2016) discussed the microbial transformation or degradation of mycotoxins with specific consideration to the detoxification mechanisms of the mother compounds by using biodegradation and/or detoxification agents. Also, in a recent review by Piotrowska (2021), the ability of mycotoxins to bind to the cell wall of microorganisms (yeasts and LAB) has been discussed.

In line with these previous studies, the focus of this review is on the biological detoxification of mycotoxins by mainly probiotic microorganisms and describes the detoxification process and the main factors influencing the stability of interactions. We conclude that if the safety of bio-decontamination is assured, a detoxification process via microorganisms can be applied instead of the currently available physical and/or chemical detoxification methods to reduce the presence of mycotoxins in foods and feeds.

Several studies have focused on the detoxification procedures for AFs, especially AFB1, with its highly toxic effects. Many strains of microorganisms reduce AFB1 in different ways, such as adsorption (Taheur et al., 2017, 2020; Piotrowska, 2021), elimination (Ejiofor et al., 2021; Piotrowska, 2021), or biotransformation (Al-Nussairawi et al., 2020; Campos-Avelar et al., 2021; Qiu et al., 2021; Shu et al., 2018; Wang et al., 2019; Watanakij et al., 2020).

Another important finding is that the binding of toxins to microorganisms is strain-specific. In general, yeasts are more efficient at detoxification than LAB. Studies have shown that the kinetics of AFB1 binding to microorganisms is rapid, indicating that neither the importation of AFB1 into the cell nor its metabolic conversion is needed. Different results were reported for the relationship between AFB1 detoxification and the viability of microorganisms, and several studies reported that the heat- and acid- treatment of microorganisms (i.e., non-viable cells) enhanced their binding abilities by protein denaturation leading to the exposure of more hydrophobic surfaces. The results of our studies (Ansari et al. 2015a,b) on AF reduction in pistachio nuts using heat-treated microorganisms from kefir grain confirm these findings but more research is needed to fully verify such achievements. The concentrations of both microorganisms and toxins are important factors that influence the AFB1 binding. As the AFB1 concentration is highly variable in different foodstuffs, selecting unique strains of microorganisms at different concentrations might lead to different results. Another important finding is that the binding process is reversible and can reach equilibrium; therefore, the concentration of AFB1 cannot reach zero under any circumstances.

7. Future perspectives

According to this literature review, further experiments are needed to demonstrate AFs–microorganism interactions in different situations. Further research is needed to develop strategies to identify appropriate microorganisms for *in vivo* studies and to prevent mycotoxin contamination. In summary, the results of these studies should provide an approach to select the most efficient microorganism (especially probiotic microorganisms) to remove mycotoxins over a wide range of concentrations. Also, the main factors affecting the stability of interactions (including strain, viability, treatment of microorganisms, and concentrations of both microorganisms and toxins) were discussed. Therefore, it is necessary to pay attention to these factors in selecting microorganisms and the detoxification process. However, the determination of food safety based on the use of viable or non-viable microorganisms during storage requires careful assessment and risk analysis.

It must be noted that most of the findings published in this literature review are related to research. Nevertheless, considering that the detoxification of food and feed using microorganisms is a low-cost method that does not require expensive equipment, this method can be used on a commercial scale. For example, the addition of *S.cerevisiae* in the mold contaminated diet on broilers ameliorated toxic effects (Ejiofor et al., 2021). In another study, a new machine was used to remove mycotoxins from a liquid beverage. This device has a probiotic LAB biofilm fixed to a cartridge. Accordingly, it allows the beverage to pass through these adsorbents, resulting in the detoxification of the liquid (Nahle et al., 2022).

Conflict of Interest

The authors declare no conflict of interest.

Ethical approval

This article contains no studies with human participants or animals performed by any of the authors.

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