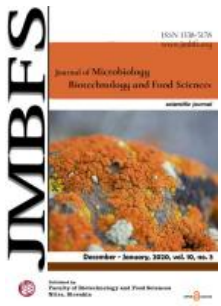

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DECONTAMINATION OF AFLATOXINS WITH A FOCUS ON AFLATOXIN B_1 BY PROBIOTIC BACTERIA AND YEASTS: A REVIEW

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ABSTRACT

Food and feed contamination by aflatoxins represents a great challenge for human and animal health. Aflatoxins detoxification using probiotic bacteria and yeasts has been introduced as an inexpensive and promising method. This article is organized with an overview of the potential application of probiotic bacteria and yeasts to eliminate, inactivate or reduce the bioavailability of aflatoxins, especially aflatoxin B_1, *in vitro* and *in vivo*. Also, a fast glance to beneficial health effects and preservative properties of probiotics followed by the mechanism of binding of aflatoxins by probiotics, influence of different probiotic pretreatments, and the stability of aflatoxin-probiotic complexes are mentioned.

Keywords: Detoxification, Probiotic, Adsoption, Aflatoxin, Stability

INTRODUCTION

Contamination of food and feed by mycotoxins is a severe problem in all countries; hence, decontamination of mycotoxins from food and feed is essential. The food and agriculture organization evaluates that approximately 25% of global food and feed are contaminated with mycotoxins (**Zoghi *et al.*, 2017**). Mycotoxins are secondary metabolites of mycelia or filamentous fungi associated to the *Penicillium*, *Aspergillus* (*A.*), and *Fusarium* genera. Production of mycotoxins may happen during the process of production, harvesting, storage or processing, under suitable temperature (between 24 and 37 °C) and humidity (above 13%) conditions (**Massoud *et al.*, 2018; Perczak *et al.*, 2018**). Several pre- and postharvest methods in order to decrease mycotoxins level in raw materials have been suggested; but, while mycotoxins levels have attained to contamination limited level in a product, it is difficult to eliminate the total toxin amount. Directly or indirectly exposure to mycotoxins may cause teratogenic, mutagenic, estrogenic, haemorrhagic, carcinogenic, immunotoxic, nephrotoxic, hepatotoxic, neurotoxic and immunosuppressive impacts on the health of animals and humans (**Haskard *et al.*, 2000; Zoghi *et al.*, 2019**).

Aflatoxins are a group of the most repeatedly found mycotoxins in a variety of foods and feeds commodities causing economic losses in industry, veterinary care costs enhancement, and livestock production decline. These toxins are secondary metabolite products of some *Aspergillus* species, especially *A. flavus*, *A. parasiticus* and *A. nomius*. Several factors affect the production of this toxin including water activity, temperature, available nutrients, competitive growth of other microorganisms, and pH-value (**Ghofrani Tabari *et al.*, 2018**). Various agricultural products may be contaminated by aflatoxins such as cereal grains especially rice, corn, maize, wheat, soya, rye, oats, barley, sorghum, nuts (almonds, peanuts, Pistachio, chestnuts, pumpkin seeds, etc.) and oily seeds such as cottonseed (**Fochesato *et al.*, 2018**). Aflatoxins can enter the human body directly or indirectly by consuming contaminated products or derived foods, such as dairy products and meats from contaminated livestock, respectively. Exposure to aflatoxins leads to severe effects on human and animal health including chronic intoxications and liver and kidney cancers (**Karazhiyan *et al.*, 2016**). Once aflatoxins are ingested by animals, they get adsorbed rapidly in the gastro intestinal tract (GIT), because they have low molecular weight, and then appear in blood and milk quickly after 15 minutes and 12 hours of post-feeding, respectively (**Martins *et al.*, 2001**).

18 types of aflatoxins are identified through toxicological studies, but the major aflatoxins are aflatoxins B_1 (AFB_1), B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2). These names are related to their fluorescence under UV light (blue (B) or green (G)) and comparative chromatographic migration patterns through thin layer chromatography (TLC) (**Lizárraga-Paulín *et al.*, 2011; Rahnama Vosough *et al.*, 2013**). *A. flavus* usually produces the B group of aflatoxins, while *A. parasiticus* produces both B and G groups of aflatoxins through several biochemical processes. Among four mentioned aflatoxins, AFB_1 is considered as the most common and dangerous one and exposure to AFB_1 leads to both acute and chronic hepatocellular injury (**Jakhar and Sadana, 2004**).

Aflatoxin M_1 (AFM_1) and aflatoxin M_2 (AFM_2) are metabolic derivates of AFB_1 and AFB_2, respectively (**Lizárraga-Paulín *et al.*, 2011**). When feed containing AFB_1 is ingested by livestock, it can be bio-transformed into AFM_1 (4-hydroxy-AFB_1) in the liver and excreted in milk, tissues, and urine of animals (**Iha *et al.*, 2013; Karazhiyan *et al.*, 2016**). AFM_1 is resistant to all stages of dairy processing including pasteurization or sterilization (**Prandini *et al.*, 2009; Assaf *et al.*, 2018**). Approximately 0.3 to 6.2% of ingested AFB_1 by livestock appears as AFM_1 in milk. Diet type, amount of milk production, breed, health, and rate of digestion can affect the change rate of AFB_1 to AFM_1. A linear relationship between the AFM_1 concentration in milk and AFB_1 in contaminated feed is reported by **Adibpour *et al.* (2016)**.

The International Agency for Research on Cancer (IARC) categorized AFB_1 and AFM_1 as group 1 that leads to human cancer (**IARC, 2016**). However AFM_1 is about ten times less toxigenic, mutagenic and genotoxic than AFB_1, its carcinogenic effects have been demonstrated in several species (**Elsanhoty *et al.*, 2014**). AFM_1 is cytotoxic and can also cause DNA damage, gene mutation, chromosomal anomalies and cell transformation in mammalians cells. The **Food and Drug Administration (2005)** recommended that the maximum acceptable level of AFM1 in milk is 0.5 µg/kg, and the **European Commission (2006)** settled this limit to 0.05 µg/kg.

Various strategies have been applied to remove aflatoxins from contaminated food and feed. Elimination of aflatoxins with chemical (addition of chlorinating, oxidizing or hydrolytic agents) and physical (UV light, heat, or ionizing radiation) approaches has some disadvantages, such as possible losses in nutritional value of treated commodities, insufficiency of toxin elimination, and requirement of expensive equipment (**Zoghi *et al.*, 2014**). In addition, one of the most effective adsorbents for AFB_1 is clay soil-based adsorbent. The layer

structure of this type of adsorbents swells when it is placed in a liquid medium and it can adsorb AFB_1 on its layers and prevent adsorption of AFB_1 by cells in the GIT (**Hadiani *et al.*, 2018a**). Nevertheless, this group of adsorbents is of low efficiency in adsorbing AFB_1. Therefore, according to the researches, bioremoval method is an interesting alternative for inexpensive control or reducing of aflatoxins in foodstuffs without losses of nutritional quality or toxic compounds generation. Probiotics are the best candidate for aflatoxins detoxification due to their GRAS (Generally recognized as safe) status.

Recently, several approaches to the removal of aflatoxins using probiotics are demonstrated. This article reviews the potential applications of probiotics in aflatoxin detoxification and the mechanism of aflatoxin binding by probiotics and the aflatoxin-probiotic complex stability are discussed.

PROBIOTICS AS AFLATOXIN BINDERS

Probiotics are described by **FAO (2016)** as 'viable microorganisms that, while ingested in sufficient amounts, exert health benefits on the host'. The main benefits for health include: lactose intolerance reduction, gut mucosal immunity support, a possible hypocholesterolemic effect, preventing the diarrheas or respiratory infections, colon cancer or inflammatory bowel disease inhibition, Helicobacter pylori or intestinal pathogens prevention, and antimutagenic and anticarcinogenic activities (**Sanders *et al.*, 2014; Yu, Chang and Lee, 2015**).

Recently, the use of microorganisms, especially probiotics, has been studied for their potential to aflatoxins elimination with an indirect health effect on the host (**Bovo *et al.*, 2012**). Several probiotic strains have been investigated for their ability to bind aflatoxins (**El-Nezami *et al.*, 1998; Bueno *et al.*, 2006; El Khoury *et al.*, 2011; El-Nezami *et al.*, 2002**).

Lactobacillus (*L.*) and *Bifidobacterium* (*B.*) species are the most known commonly probiotic bacteria, as well as the yeast *Saccharomyces* (*S.*) *cerevisiae* and *Bacillus* species and some strains of *Escherichia (E.) coli*. A functional classification of nontoxigenic, nonpathogenic, and fermentative probiotic bacteria are Lactic acid bacteria (LAB) witch are mainly related to the human gastrointestinal tract and widely used in food industry (**Zoghi *et al.*, 2017**). LAB are Gram-positive, organotrophic, nonsporulating, fermentative rods or cocci, air and acid tolerant, which produce mostly lactic acid as the end-product of carbohydrate fermentation. All of them are anaerobic, but some of them can tolerate low levels of oxygen. *Enterococcus*, *Lactococcus*, *Pediococcus*, *Oenococcus*, *Leuconostoc*, *Streptococcus*, and *Lactobacillus* species are industrially important genera. The genus *Bifidobacteria* is also used as LAB, however they are phylogenetically unrelated and have unique sugar fermentation pathways. LAB are widely used in the world food production, vegetables, meat, and fermented dairy products. LAB play a significant role in improving the flavour, texture, and shelf-life of food products (**Perczak *et al.*, 2018**).

It is demonstrated that living and dead probiotics are able to decontaminate aflatoxins by attaching the toxin to their cell wall components. This phenomenon can be described as adsorption by components of the cell wall rather than by metabolism or covalent binding (**Santos *et al.*, 2006**). Capability of nonviable probiotics in aflatoxins decontamination is an important point of view because the viability of probiotics decreases under low pH condition through passing the stomach (**Topcu *et al.*, 2010; Hamidi *et al.*, 2013**). **El-Nezami *et al.* (1998)** reported that five strains of *Lactobacillus* and one *Propionibacterium* were significantly effective in aflatoxin removal from aqueous solution in comparison to *E. coli*. In another study, **Peltonen *et al.* (2001)** stated that significant differences in the binding abilities of different amounts of AFB_1 were due to different bacterial cell wall structures.

Inhibition of aflatoxin biosynthesis by LAB

A few authors also reported the antifungal properties of LAB. The main LAB recognized for this ability belong to *Lactococcus* and *Lactobacillus* (*L.*) genera. In contrast, it is reported that some LAB strains such as *L. lactis* can motivate aflatoxin accumulation. **Coallier-Ascah and Idziak (1985)** demonstrated a significant inhibition of aflatoxin accumulation by LAB and reported that this inhibition was not related to a pH decrease or a hydrogen peroxide production but rather to producing a heat stable and low molecular weight metabolite by LAB at the beginning of its growth phase. **Gourama and Bullerman (1997)** also reported that prevention of aflatoxin synthesis by *Lactobacillus* strain was due to specific bacterial metabolites. Several effective parameters related to antifungal properties of LAB have been investigated including growth medium, temperature, incubation time, pH, and nutritional factors. It was revealed that temperature and period of incubation were significantly affecting the amounts of antifungal metabolite production (**Dalié *et al.*, 2010**). **Gonzalez Pereyra *et al.* (2018)** found that six *Bacillus* sp. strains were capable of decrease aflatoxigenic *A. parasiticus* growth rate significantly and could also decrease AFB_1 concentration.

FACTORS AFFECTING AFLATOXIN BIOREMOVAL BY PROBIOTICS

Several criteria affect the aflatoxins removal using probiotics such as probiotic strain concentration and specificity, toxin concentration, pH, and incubation time.

Effect of probiotic strain specificity and concentration

In addition to bacterial strain specificity, the bacterial concentration can also affect the aflatoxin removal. Detoxification of aflatoxins by viable or nonviable probiotic cells is strain dependent (**Topcu *et al.*, 2010**). In some studies, LAB were considered to be inappropriate binders of AFB_1. This may be due to the specific LAB strains used in those studies (**Shetty and Jespersen, 2006**). Similarly, **Peltonen *et al.* (2001)** assayed 20 LAB strains and reported that the differences in AFB_1 binding were because of different bacterial strain specificity. So, differences between aflatoxin ability of strains of LAB indicate that binding ability is highly strain dependent. **El-Nezami *et al.* (1998)** showed that *L. rhamnosus* strains GG and LC 705 can significantly remove AFB1 in comparison to other strains of LAB and the removal process was bacterial concentration dependent.

Toxin concentration effect

Several researchers such as **El-Nezami *et al.* (1998)**, **Elsanhoty *et al.* (2014)** and **Peltonen *et al.* (2001)** reported that the amounts of aflatoxin removed by viable and nonviable bacteria depend on initial toxin concentrations. In addition, **Pizzolitto *et al.* (2012)** demonstrated that the removal of AFB_1 depended on the LAB strain; because some of LAB strains were more efficient at a low toxin concentration (*L. rhamnosus* at 50 ppb) and other applied LAB were more efficient at high AFB_1 concentration (*L. acidophilus* at 100 ppb and *L. casei* at 500 ppb). According to **Shetty *et al.* (2007)** the absolute amount of the AFB_1 removal increased steadily with increasing concentration of AFB_1; therefore, the initial AFB_1 concentration had a considerable impact on the binding capacity. In contrast, **Rahayu *et al.* (2007)** stated that AFB_1 concentration enhancement did not affect the percentage of AFB_1 binding; but, it influenced the binding speed. Also, **Lee *et al.* (2003)** reported AFB_1 binding as a linear process and dependent on the toxin concentration at low level of AFB_1, and a plateau process at higher toxin concentrations.

Effect of pH-value

Some investigation showed that binding process is not pH dependent exclusively. According to **Zinedine *et al.* (2005)** all the assayed *Lactobacillus* spp. removed AFB_1 from 5% to 40% when pH increased from 3 to 5.5. Also, **Pranoto *et al.* (2007)** demonstrated that amount of bound AFB_1 by LAB was higher at low pH (< 5) in compare with pH 6 and 7. In another study, **Rayes (2013)** stated that at pH 8.5 the highest decrease percentage of AFB_1 by a pool of LAB occurred, while at pH 4.5 the lowest removal observed. On the other hand, the highest and lowest AFB_1 removal was at pH 4.5 and 8.5, respectively, when the pool was included a *S. cerevisiae* strain. **Hernandez-Mendoza *et al.* (2009)** investigated the binding of *L. reuteri* and *L. casei* with AFB_1 at different pH (6, 7.2, and 8) and incubation time (4 and 12 h). They showed that the highest AFB1-binding capacity was at pH 7.2. Furthermore, **Topcu *et al.* (2010)** found that the binding of AFB_1 by *Enterococcus faecium* was a pH and incubation time dependent process. In contrast, **Bovo *et al.* (2014)** showed no significant differences in the AFB_1 reduction between *L. rhamnosus* strains conditions (spray, in solution or freeze-dried) at pH 3 and 6. So, it can be concluded that the pH dependence of AFB_1 binding vary between bacterial strains. In addition, binding of AFB_1 in a study, was not affected by pH, but binding of AFB_2 considerably influenced by pH. It indicates that different metabolites of the same mycotoxin may show significant differences depend on binding mechanisms.

Effect of incubation time

Peltonen *et al.* (2001) stated that the AFB_1 binding by *L. amylovorus* CSCC 5197 was a fast process and increased from 52% (0 h) to 73.2% (72 h). Similarly, **Topcu *et al.* (2010)** reported that *Enterococcus faecium* M74 and EF031 strains at 1 h removed almost 65% of the total AFB_1 removed during the whole incubation period (48 h). Bovo et al. (2012) stated that some probiotic strains bound AFM_1 from skimmed milk in 15 min within a range from 13.51 to 37.75%. In another study, it was reported that the percentage of AFB_1 removal was not significantly different between the 0 h and 72 h incubation period (**Pizzolitto *et al.*, 2012**). In addition, **El-Nezami *et al.* (1998)** showed that the AFB_1 removal was fast and no significant different was observed between different incubation times. **Motawee and El- Ghany (2011)** noted that the percentage of AFM_1 and AFB_1 reduction after 5 h by eight dairy strains of LAB in yoghurt was not considerably less than the whole of storage time. These results suggest that the binding of AFB_1 by probiotics is a rapid process and the removal does not increase with the incubation time, considerably.

BINDING OF AFLATOXINS BY LAB

Specific strains of LAB are generally the most known probiotics for reducing aflatoxins. It has been reported that different strains of LAB have different effect on AFB_1 removal *in vitro*. This removal is due to binding of bacterial cell wall to the aflatoxin, not bacterial metabolism. It was described that *in vitro* binding of

AFB_1 by LAB is a fast (less than 1 min), strain specific, and reversible process (**Bueno *et al.*, 2006; Kankaanpaa *et al.*, 2000**).

El Nezami *et al.* (1998) assayed the capacity of *L. rhamnosus* GG, *L. rhamnosus* LC705, *L. acidophilus*, *L. gasseri*, *L. casei* Shirota, and *Propionibacterium freudenreichii* ssp. *shermanii* JS to bind AFB_1 in a liquid medium and stated that *L. rhamnosus* strains GG and LC705 removed 80% of the toxin. They emphasized that the viability of cells was not a perquisite for this binding capacity. Then, **Haskard *et al.* (2001)** tested 12 viable and non-viable LAB strains and found that *L. rhamnosus* was the best strain to remove AFB_1. The authors demonstrated that some surface components of the LAB were involved in binding. Also, **Peltonen *et al.* (2001)** investigated the binding of AFB_1 by 12 *Lactobacillus*, five *Bifidobacterium* and three *Lactococcus* strains and revealed that two strains of *L. amylovorus* and *L. rhamnosus* removed more than 50% of initial AFB_1 concentration. In addition, **Motameny *et al.* (2012)** studied the AFB_1 removal from a gastrointestinal model by *L. rhamnosus*, *L. plantarum*, and *L. acidophilus* and found that all strains were able to AFB_1 detoxification and *L. plantarum* was the most successful (28 %). **Elsanhoty *et al.* (2014)** reported that *L. rhamnosus* was the most effective in the binding of AFB_1, AFB_2, AFG_1, and AFG_2 from liquid medium in compared with *L. acidophilus*, *L. sanfranciscensis*, and *B. angulatum* and LAB-aflatoxin complex was stable. On the other hand, **Sarimehmetoglu and Küplülü (2004)** compared the ability of *Streptococcus thermophilus* ST-36 and *L. delbrueckii ssp. bulgaricus* CH-2 to AFM_1 removal from phosphate buffer saline (PBS) and milk. **Elgerbi *et al.* (2006)** found that the percentage of AFM_1 binding by *Lactobacillus* spp., *Lactococcus* spp. and *Bifidobacterium* spp. ranged from 4.5-73.1% after 96 hr.

Sezer *et al.* (2013) reported that *L. plantarum* was more efficient than *L. lactis* in removing AFB_1 from liquid culture (46% and 27%, respectively), but when the two strains were combined, AFB_1 removal reached 81%. **Corassin *et al.* (2013)** also revealed that a combination of LAB (*L. rhamnosus*, *L. delbrueckii*, and *B. lactis*) and *S. cerevisiae* could reduce AFM_1 from UHT skim milk, completely. In contrast, **El-Khoury *et al.* (2011)** stated that *L. bulgaricus*, *Streptococcus thermophilus* and a mixture of these two bacterium reduced AFM_1 content of milk to 58.5, 37.7 and 46.7%, respectively. It can be concluded that combination of specific probiotic strains may lead to a more aflatoxin removal efficiency than a single one, but may reduce their toxin removal capacity.

Some authors have reported a mathematical model to illustrate the *in vitro* AFB_1 binding to the LAB cell wall. A theoretical model has been suggested by **Bueno *et al.* (2006)**. This model takes two possible processes into investigation: adsorption (binding) and desorption (release) of AFB_1 to and from the binding site on the LAB surface. This model shows that AFB_1 binds to a number of sites in LAB and allows us to evaluate the number of AFB_1 binding sites and the efficacy of cells to reduce AFB_1 from a liquid medium. So, this model demonstrates that the different abilities of probiotic strains to bind AFB_1 are directly link to the number of binding sites of each probiotic.

BINDING OF AFLATOXINS BY YEASTS

Data found in the literature indicate that in addition to LAB, other organisms such as *S. cerevisiae* have the potential to bind aflatoxins. Yeast cells can bind to different molecules such as toxins as complexes on their cell wall surfaces (**Baptista *et al.*, 2004**). **Corassin *et al.* (2013)** evaluated the AFM_1 binding ability of *L. rhamnosus*, *L. delbrueckii* spp. *bulgaricus*, and *B. lactis* in combination with heat-treated *S. cerevisiae*. This mixture could bind with 100% of AFM_1. In a study, *S. cerevisiae* and *Candida krusei* were tested for AFB_1 binding and they could bind more than 60% (w/w) of the added mycotoxins in PBS. They emphasized the AFB_1 binding was highly strain specific (**Shetty and Jespersen, 2006**). In another research, when dried yeast and yeast cell wall (include mannan-oligosaccharides) with AFB_1 were added to rat-ration feed, a significant decrease in the toxicity was observed (**Baptista *et al.*, 2004**).

MECHANISM OF AFLATOXIN BINDING BY PROBIOTICS

Several researchers studied the mechanism of binding of aflatoxins to probiotics. A review by **Shetty and Jespersen (2006)** stated that aflatoxin removal by probiotics is due to adhesion to cell wall components, because nonviable and viable probiotics are able to remove aflatoxins *in vitro* with similar efficiency. Possible binding sites include carbohydrates, proteins or a combination of both.

It has been shown that two main components responsible for the binding of AFB_1 by *L. rhamnosus* GG are cell wall polysaccharide and peptidoglycan. In addition, since LAB strain treatment with lipases did not lead to a significant increase in AFB_1 binding, it was supposed that no fatty acids were involved in this adsorption (**Lahtinen *et al.*, 2004**). Similarly, other authors have suggested that the peptidoglycan of LAB is the most likely site of aflatoxins binding (**Haskard *et al.*, 2000; Niderkorn *et al.*, 2009**). **Yiannikouris *et al.* (2006)** found that a cell wall component of many microorganisms named beta-d-glucans, played a key in the binding of aflatoxins. Recently, it was reported that the binding characteristics of a probiotic strain are possibly depend on the exopolysaccharides produced by the probiotics (**Taheur *et al.*, 2017**). Also, **Haskard *et al.* (2001)** indicated superior involvement of hydrophobic interactions and main role of teichoic acids in aflatoxin binding mechanism. Similarly, **Hernandez-Mendoza *et al.* (2009)** showed that teichoic acids as well as peptidoglycans were important parts of the cell wall which could bind aflatoxin. Another report indicated the main role of teichoic acids in aflatoxin binding by probiotics. Teichoic acids may contribute mainly to hydrophobicity of wall contributed by anionic carbohydrates (**Gratz *et al.*, 2004**). It can be concluded that binding of probiotics to aflatoxins is a function of fibril network of teichoic acids, peptidoglycans, and polysaccharides. Another mechanistic study conducted by **Fochesato *et al.* (2018)**, which demonstrated that polysaccharides of *L. rhamnosus* attached aflatoxins. These polysaccharides are in three principal forms: peptidoglycan, cell wall polysaccharide, and teichoic or lipoteichoic acids. The environmental conditions such as pH-value or enzymes would be affecting the three-dimensional structure of the cell wall and the binding sites for aflatoxins. Therefore, it can be concluded that aflatoxin removal is due to the physical binding rather than metabolism, because peptidogylcan is one of the three principal carbohydrate forms of bacterial cell wall.

When acid or heat treatments were used for LAB, it has been demonstrated that LAB ability to remove AFB_1 increased. Also, inserting some basic compounds such as NaOH, Na_2CO_3, and isopropanol had negative influence on this binding (**El-Nezami *et al.*, 1998**). **Haskard *et al.* (2000)** investigated the mechanism of binding of *L. rhamnosus* to aflatoxins. They used pronase E and periodate treatments (using periodate causes oxidation of cis OH groups to aldehydes and carbon acid groups) on viable, heat and acid-inactivated probiotic strains and suggested that binding was due to carbohydrate and protein components in cell wall, because a considerable decrease in AFB_1 binding was observed. Heat and acid treatments cause protein denaturation and lead to the exposure of more hydrophobic surfaces. They also reported that AFB_1 binding reduction by urea-treated LAB indicated the key role of hydrophobic interactions in binding. On the other hand, treatments with metal ions such as Na^+ and Ca^{2+} showed that electrostatic interactions and hydrogen bonding played only minor role in AFB_1 binding by LAB, because this process was not affected by mono and divalent ions or by changes in pH (2.5–8.5).

LAB cell wall

Some authors suggested that the significant differences among aflatoxin binding ability of LAB depends on different cell wall structures (**El-Nezami *et al.*, 1998; Peltonen *et al.*, 2001; Zinedine *et al.*, 2005; Hernandez-Mendoza *et al.*, 2009; Lahtinen *et al.*, 2004; Pierides *et al.*, 2000**). Cell wall structure of LAB is reviewed widely by several researchers (**Chapot-Chartier and Kulakauskas, 2014; Elsanhoty *et al.*, 2016; Zoghi *et al.*, 2017; Liu *et al.*, 2018; Zoghi *et al.*, 2019; Nazareth *et al.*, 2020**).

Heterogeneous bacteria of LAB, posses a typical gram positive cell wall containing the peptidoglycan matrices, organic acids (teichoic and lipoteichoic acid), proteinacious surface (S) layer and neutral polysaccharides. These components play various functions including adhesion to macromolecules such as toxins (**Perczak *et al.*, 2018**). Cell wall polysaccharides are produced by LAB with large variation between different strains (**Zoghi *et al.*, 2014**). The peptidoglycan consists of polymerized disaccharide N-acetyl-glucosamine-beta (1-4)-N-acetyl muramic acid chains cross-linked by pentapeptide bridges. Disaccharide units of peptidoglycan have three different amendments, including acetyl groups of both N-acetyl-glucosamine and N-acetyl- muramic acid. Some LAB strains such as *Enterococcus faecium*, *Pediococcus pentosaceus*, *L. plantarum*, and *L. casei* have a diverging amino acid sequence of pentapeptide bridge where c-terminal d-alanine is replaced by d-lactate (**Grohs *et al.*, 2004**).

Teichoic acids are anionic polymers which bind to the peptidoglycan layer via a linkage unit and contribute more than 50% (w/w) of total weight of cell wall. The structure of the linkage unit is glycerol-phospho-N-acetyl mannosaminyl-beta (1-4)- glucosamine. Two types of teichoic acids which are detected from LAB, including poly glycerol phosphate and poly ribitol phosphate teichoic acids. Lipoteichoic acids are structurally similar to teichoic acids but they attach to the plasma membrane instead of peptidoglycan by a glycolipid anchor. The most frequently identified lipoteichoic acid in LAB is the poly glycerol phosphate lipoteichoic acid, which is almost similar to the structure of poly glycerol phosphate teichoic acid (**Ambrosini *et al.*, 1996**). Some LAB strains such as *Lactobacillus*, *Enterococcus*, *Sterptococcus*, *Bifidobacterium* and *Propionibacterium* produce exopolysaccharides containing glucose, rhamnose, galactose, mannose, N-acetylgalactosamine, and N-acetylglucosamine (**Grohs *et al.*, 2004**). Many LAB from the genus *Lactobacillus* are able to produce S-layer proteins. The size of these proteins is 25-50 kDa with calculated pI's ranging from 9.35 to 10.88, and they are highly basic. LAB which cannot produce S-layer proteins have a negative surface charge at neutral pH. Also, it has been reported that the surface charge of S-layer producing *Lactobacillus* are negative. This phenomenon may be due to the involvement of positively charged areas of S-layer proteins in their adhesion to peptidoglycan (**Zoghi *et al.*, 2014**).

S. cereviciae cell wall

Except LAB, *S. cereviciae* is reported to the most used yeast as a probiotic strain in order to aflatoxins removal. *S. cerevisiae* cell wall represents about 30% (w/w) of total weight of the cell and made up of a network of back bone of β-1,3 glucan

with β-1,6 glucan side chains, which is covalently linked to glycosylated mannoproteins. The cell wall mannoprotein includes a very heterogeneous class of glycoproteins. Carbohydrate fraction represents as much as 90% (w/w) of mannoproteins and oligosaccharide of mannan constitutes approximately 50% w/w of the total carbohydrates (**Hadiani *et al.*, 2018b**). The core contains mannoproteins and branched mannose side chains as well as short and rigid rods like clusters of oligomannosyl chains extend out. Phosphodiester bridges in mannosyl side chains contribute negative charges on the cell surface. In addition, the cell wall of *S. cereviciae* is a highly dynamic structure which quickly replies to changes in the environmental stresses (**Zoghi *et al.*, 2014**). Based on chemical combination and physical nature of cell wall of *S. cerevisiae*, it can be concluded that cell surface presents limitless sites on it in order to physical adsorption of aflatoxins.

According to certain research, it is confirmed that mannan components of the cell wall play a main role in aflatoxin binding by *S. cerevisiae* (**Shetty and Jespersen, 2006**). The proteins and glucans provide accessible adsorption sites with ability to adsorb aflatoxins through various mechanisms such as hydrogen bonds and ionic or hydrophobic reactions. Heat treatment of *S. cerevisiae* increases permeability of the outer layer of cell wall, due to dissolution of cell-surface mannan and development of adsorption regions (**Shetty *et al.*, 2007**).

EFFECT OF DIFFERENT PROBIOTIC PRETREATMENTS ON AFLATOXIN BINDING

Haskard *et al.* (2001) revealed that using heat treatment for *L. rhamnosus* GG and LC 705 strains led to significant increase in AFB_1 removal from contaminated defined medium and the stability of LAB-AFB_1 complex. Similarly, **Elsanhoty *et al.* (2014)** found that heat treatment of *L. rhamnosus* can significantly enhance its binding to AFM_1 in yoghurt. Reported literature indicates that heat treatment of LAB exhibit higher removal capacity, because of changes on the cell surface (**Perczak *et al.*, 2018**). Other researchers showed that heat treated yeast reduce aflatoxins more than viable cells. Heating is responsible for protein denaturation or the formation of Maillard reaction products in the cell wall (**Shetty *et al.*, 2007; Rahaie *et al.*, 2010**).

Several researchers showed that the acid treatment of yeast or LAB caused the highest adsorption of aflatoxin compared with viable and heat-treated probiotic (**Haskard *et al.*, 2001; Rahaie *et al.*, 2010; Hegazy *et al.*, 2011**). **El-Nezami *et al.* (1998)** reported that the binding ability of LAB increased by acid pretreatment. They also stated that acid treatment might break amine linkage in peptides and proteins, producing peptides and amino acids. Moreover, accessible aflatoxin binding sites increase and allow the aflatoxins to bind to the cell wall or its associated components (**El-Nezami *et al.*, 2002**). According to **Haskard *et al.* (2001)** acid treatment may affect cell wall components such as peptidoglycan and polysaccharide by releasing monomers and further fragmentation into aldehydes after the glycosidic linkages break down. The acidic conditions could make AFB_1 to be easily and repidly bound by constituents of cytoplasmic membrane (**Bejaoui *et al.*, 2004**). Furthermore, **Haskard *et al.* (2000)** noted that hydrophobic interactions were expected in acid-treated LAB; because the protein denaturation may exhibit more hydrophobic binding areas to aflatoxins.

In another study, significant increase in the ability of *L. rhamnosus* GG to bind AFB_1 was observed after treatment with sodium dodecyl sulphate, whereas, treatment with urea showed no effect. One of the probable reasons could be the denaturation of protein by sodium dodecyl sulphate and cell wall isolation consist of peptidoglycan. The exposure of *L. rhamnosus* GG to divalent cations such as Ca^{2+} and Mg^{2+} or chelators such as EDTA and ethylene glycol tetra-acetic acid, as well as sonication and enzymatic treatments include different specific proteases, did not affect the binding of AFB_1 may be due to the release of molecules bound to the surface of the bacteria (**Lahtinen *et al.*, 2004**).

In fact, probiotic pretreatments which lead to protein denaturation, release of some components, and increase of pore size, probably act on the charge distribution change and hydrophobic nature of the bacterial surface and therefore enhance the efficiency of probiotics as adsorbent of aflatoxin (**Karazhiyan *et al.*, 2016; Ahlberg *et al.*, 2015**).

PROBIOTIC-AFLATOXIN COMPLEX STABILITY

Several researchers have reported the partial reversibility of the process of probiotics binding by probiotics (**Peltonen *et al.*, 2001; Hernandez-Mendoza *et al.*, 2009**); **Haskard *et al.* (2001)** studied the stability of 12 LAB-AFB_1 complexes in both viable and nonviable forms (heat and acid treated LAB) after five washing steps with water. They exhibited that up to 71% of the total AFB_1 remained bound and binding of aflatoxins to cell surface is significantly strong. In their investigation, viable cells of *L. rhamnosus* strains LGG and LC105 retained 38 and 50% (w/w) of the bound AFB_1, respectively. Whereas, non-viable (acid and heat treated) cells retained the highest amount of AFB_1 (66–71% (w/w)). Also, they revealed that autoclaving and sonication treated probiotic bacteria did not release any detectable AFB_1. The authors concluded that the binding was reversible, but the stability of the complexes depended on strain, treatment and environmental conditions.

Hernandez-Mendoza *et al.* (2009) reported that about 60–70% of AFB_1 remained bound to the probiotic cells after washing by PBS; so, AFB_1 attached to the bacteria by almost weak and partially reversible bound. **Pizzolitto *et al.* (2012)** stated that after five washings with PBS, different LAB cells retained AFB_1 bound close to 50%, and the washing time (1-60 min) did not affect the release percentages. Among a panel of native LAB isolated from Iranian sourdough and dairy products, *L. casei* was reported to have the strongest binding of aflatoxin compared to other *L. plantarum* and *L. fermentum* strains (**Fazeli *et al.*, 2009**). According to the findings obtained from the washing of AFB_1–*Enterococcus faecium* complex, the binding of AFB_1 to bacterial cell surface was a reversible process and the stability of the complexes was strain specific (**Topcu *et al.*, 2010**). Similarly, it was noted that after washing the AFB_1-*Lactobacillus* complexes, variable amounts of AFB_1 were released back into the solution (**Peltonen *et al.*, 2001**). Also, the stability of AFB_1-*Enterococcus faecium* strains (MF4 and GJ40) complexes was found to be high after three washes with PBS (**Fernandez Juri *et al.*, 2014**). In addition, a stable AFM_1-LAB (*L. rhamnosus* and *L. plantarum*) complex was showed by **Elsanhoty *et al.* (2014)**. Moreover, **Bevilacqua *et al.* (2014)** described the proportionality of the amount of aflatoxin released into the medium by the number of treatments performed.

According to the above discussion, it is clear that any *in vitro* results must be supported by *in vivo* experiments, because aflatoxins may be released by the continual washing of the bacterial surface in the GIT and negative health implications may be observed. Thus, several studies have attempted to evaluate the stability of the aflatoxin-probiotic complexes in the GIT conditions. It is revealed that defined LAB that show significant adhesion to intestinal cells lose this property when they bind to aflatoxins. Therefore, in the gastrointestinal tract, the bacteria–aflatoxin complex is rapidly excreted (**Gratz *et al.*, 2004**).

IN VIVO STUDIES

Many recent studies revealed that AFB_1 intake can change the morphological and immune function of the intestinal mucosa due to decreasing the percentage of T-cell subsets and the expression level of cytokine mRNA in the small intestine. The mechanism of intestinal tissue poisoning of the host by AFB_1 includes the prevention of oxygen production and inhibition of the free radicals of oxygen (**Jiang *et al.*, 2015**). Intestinal cells can absorb aflatoxins at high rates (>80%), regardless of the species (**Grenier and Applegate, 2013; Wan *et al.*, 2016**). Some experimental evidences reported that probiotics could bind aflatoxins within the lumen, so, reducing the negative impacts of aflatoxins and improving gut and liver health (**Niderkorn *et al.*, 2009; Gratz *et al.*, 2010**).

A few investigations by **Slizewska *et al.* (2010)**, **Hathout *et al.* (2011)**, **Nikbakht Nasrabadi *et al.* (2013)**, and **Yadav *et al.* (2013)** indicated the ability of probiotics to decrease genotoxicity impacts and protect animals against oxidative stresses. **Hathout *et al.* (2011)** showed that *L. reuteri* and *L. casei* were able to considerably reduce malondialdehyde concentration in the kidney and liver. As aflatoxin toxicity is mainly related to the liver, using probiotics could improve the histological picture and architecture of the liver and serum biochemical parameters.

Besides *in vitro* studies, the AFB_1 binding ability of probiotics was evaluated *ex vivo* in the intestinal lumen of chicken using the chicken duodenum loop technique (**El-Nezami *et al.*, 2000**). The authors stated that *L. rhamnosus* GG, *L. rhamnosus* LC705, and *Propionibacterium freudenreichii* removed 54, 44, and 36% of the AFB_1, respectively from the soluble fraction of the luminal fluid within 1 min. It can be concluded from these findings that AFB_1 binding by LAB appears in physiological conditions in animals, which may represents a way to reduce AFB_1 bioavailability in the organism. **El Nezami *et al.* (2006)** continued their research in Egypt and investigated the effect of a combination of *L. rhamnosus* LC705 and *Propionibacterium freudenreichii* on AFB_1 levels in human feces samples from 20 healthy volunteers. The mentioned probiotic strains were administered two times per day (at a dosage of $2\text{-}5\times10^{10}$ CFU/day) for five weeks by volunteers and the control group received a placebo. The marker for biologically effective dose of AFB_1 was the adduct AFB_1-N7-guanine. High level of this adduct in the urinary excretion is associated to a high risk of liver cancer (**Vinderola and Ritieni, 2015**). The fecal samples were positive for AFB_1 with a range from 1.8 to 6 μg AFB_1/kg feces for 11 volunteers. A significant reduction in urinary excretion of AFB_1- N7-guanine and fecal aflatoxin levels was observed for volunteers after receiving the probiotic mixture compared to volunteers receiving a placebo.

Kankaanpaa *et al.* (2000) showed that aflatoxin binding by *L. rhamnosus* LGG and LC105 considerably reduced adhesion properties of the probiotic strains and facilitates excretion of immobilized AFB_1. Similarly, **Gratz *et al.* (2004)** reported that pre-exposure of *L. rhamnosus* GG to AFB_1 decreases its binding with intestinal mucus and leads to faster removal. Also, it was shown that addition of *S. cerevisiae* to the animal diet reduced aflatoxin toxicities; thus, possible stability of the yeast-afflatoxin complex was indicated through the GIT (**Shetty and Jespersen, 2006; Armando *et al.*, 2012**). Similar results reported by **Gratz *et al.* (2006)** who found that *L. rhamnosus* GG was able to modulate AFB_1 uptake in rats, increased fecal AFB_1 excretion in rats and reduced liver injury. As demonstrated, *L. casei* Shirota can decrease AFB_1 absorption in the GIT even after a long period of toxin exposure (**Hernandez-Mendoza *et al.*, 2010**).

Nikbakht Nasrabadi *et al.* (2013) also found that *L. casei* Shirota could reduce the blood serum level of AFB_1 in rats and improved the adverse effect of AFB_1 on rats' body weight and plasma biochemical parameters. This result is consistent with **Hernandez-Mendoza *et al.* (2009)** who stated that *L. reuteri* was able to bind to AFB_1 in all intestinal sections under normal conditions of the GIT. On the other hand, another study revealed that the probiotic mixture could only retard the AFB_1 absorption in duodenal loops and considerably decrease the AFB_1 adsorption in the intestinal mucus (**Gratz *et al.*, 2005**).
Fochesato *et al.* (2018) reported that dynamics of AFB_1 adsorption and desorption by *L. rhamnosus* RC007 were strongly affected by the salivary environment. The knowledge of the adsorption dynamics of AFB_1 with a probiotic strain will allow predicting its behavior at each stage of the GIT.

CONCLUSION

Aflatoxins frequently contaminate the food and feed at various levels. So, for the food industry, it has always been an uphill task to control the aflatoxins level in the products. It is suggested that probiotic strains with high aflatoxin binding abilities can be used in food industries as additives in small quantities without compromising the characteristics of the final product and thus can avoid accumulation of this toxic compound and decrease its toxic effects. Many studies have demonstrated varying efficiency of some selected probiotics in removing aflatoxins. Tables 1 and 2 demonstrate several kinds of probiotics applied for decontamination of food and feed from AFB_1 and AFM_1, respectively.

Table 1 Several kinds of probiotics applied for decontamination of aflatoxin B_1

Probiotic species	Strain	Medium kind	Probiotic concentration (CFU/mL)	Probiotic Condition	Initial AFB_1 Concentration	AFB_1 removal %	Explanation	Reference
Flavobacterium aurantiacum	NRRL B-184	aqueous solution		Viable Heat-treated Proteinase-treated DNase-treated	2 ppm	74.5 55 34.5 80.5	At 30 °C for 24 h	Smiley & Draughon, 2000
L. acidophilus *L. casei Shirota* *L. gasseri* *L. rhamnosus* *L. rhamnosus*	ATCC 4356 YIT 9018 ATCC 33323 GG LC-705	Liquid media		Viable Heat-treated	5,10,50 mg/mL	55-67 33-58 48-68 75-82 75-82	0-72 h incubation period at 37 °C. Toxin concentration and temperature dependent process	El-Nezami et al., 1998
S. cerevisiae		aqueous solution	2×10^8	Viable Acid-treated Cell wall	2 ppm	44.45 73.35 73.03		Ghofrani Tabari et al., 2018
L. rhamnosus	GG	aqueous solution	1×10^9	Viable Acid-treated Cell wall	2 ppm	46.46 75.52 75.28		Ghofrani Tabari et al., 2018
Enterococcus faecium	EF031 M74	aqueous solution	1×10^{10}	Viable non-viable	5 mg/L	23.4 - 37.5 19.3-30.5	48 h incubation period pH 7	Topcu et al., 2010
Enterococcus faecium	GJ40	aqueous solution	1×10^8	Viable heat-killed cells	50 ppb 100 ppb	24–27 17–24	48 h incubation period pH 7	Fernandez Juri et al., 2014
Enterococcus faecium	MF4	aqueous solution	1×10^8	Viable heat-killed cells	50 ppb 100 ppb	36–42 27–32	48 h incubation period pH 7	Fernandez Juri et al., 2014
Lactobacillus sp.	G7 PDS3	aqueous solution	1×10^{10}	Viable nonviable	5 mg/L	69.11 73.75	48 h incubation period	Damayanti et al., 2017
L. rhamnosus	RC007	Simulated GIT	1×10^8	viable	93.89 ng/g	82.39	Under GIT conditions	Fochesato et al., 2018
L. rhamnosus	GG	cottonseed	1×10^9	Viable heat killed acid killed	5 µg/L 10 µg/L 20 µg/L	44-49	slow process 24 h incubation period	Rahnama Vosough et al., 2013
Lactococcus lactis *Sterptococcus thermophilus*		phosphate buffer solution	$10^7 – 10^8$	Dead cells (by boiling)	2 µg/L	86.1 100	Strong stability of complex	Shahin, 2007
Lactococcus lactis *Sterptococcus thermophilus*		phosphate buffer solution	$10^7 – 10^8$	viable	2 µg/L	54.35 81	Strong stability	Shahin, 2007
L. kefiri	KFLM3	milk	8.4×10^7	viable	1 µg/mL	80-100		Taheur et al., 2017
L. acidophilus	E-94507 CSCC 5361	aqueous solution	1×10^{10}	viable	2 mg/mL	18.2 20.7	24 h incubation period at 37 °C.	Peltonen et al., 2001
L. amylovorus	CSCC 5197 CSCC 5160	aqueous solution	1×10^{10}	viable	2 mg/mL	57.8 59.7	24 h incubation period at 37 °C.	Peltonen et al., 2001
L. delbrueckii subsp. bulgaricus *L. helveticus* *L. fermentum* *L. johnsonii* *L. plantarum* *B. Lactis* *B. Longum*	CSCC 5142 E-79098 CSCC 5094 CSCC 5304 CSCC 1941	aqueous solution	1×10^{10}	viable	2 mg/mL	17.3 34.2 22.6 30.1 28.4 48.7 37.5 45.7	24 h incubation period at 37 °C. Reversible binding	Peltonen et al., 2001

B. animalis								
L. acidophilus *S. cerevisiae*	24 CECT 1891	liquid medium	1×10^{7}- 8×10^{9}	viable	1.5; 3.75; 7.5; 15 µg/mL	15-24		Pizzolitto et al., 2012
L. paracasei *L. brevis* *L. plantarum* *S. cerevisiae*	LOCK0920 LOCK0944 LOCK0945 LOCK0140	Fecal water		hydrogen peroxide-treated		22		Slizewska et al., 2010
L. brevis		Maize grain		Heat-treated viable	80 ng/g	33-75 33	72 h incubation period	Oluwafemi & Da-Silva, 2009
L. delbrueckii subsp. bulgaricus		Maize grain		Viable Heat killed	80 ng/g	50 56	72 h incubation period	Oluwafemi & Da-Silva, 2009
L. plantarum		Maize grain		Viable Heat killed		75 95	48 h incubation period	Oluwafemi et al., 2010
L. casei *L. casei* *B. bifidum*	Shirota Defensis	aqueous solution	$2\text{-}3\times10^{9}$	viable	4.6 µg /mL	15-68 35-60 35-60	4 & 12 h incubation period	Hernandez-Mendoza et al., 2009
S. cerevisiae		Corn for mice feed		viable		72	6 weeks incubation period	Motameny et al., 2012
S. cerevisiae	A 18 26.1.11	Indigenous fermented foods	1×10^{9}	Viable, heat and acid treated cells	1 to 20 µg/mL	53 48	20 to 37 °C	Shetty et al., 2007
L. rhamnosus	GG	Aqueous solution		viable		61	Time-dependent process	Gratz et al., 2007
L. plantarum	PTCC 1058			viable		45 100	1 h incubation period 90 h incubation period	Khanafari et al., 2007
L. johnsonii *L. paracasei* *L. salivarius* *B. lactis*	LM2-118 Bb-12			viable		38.8 30 17 18	24 h incubation period	Peltonen et al., 2000
L.casei *B. bifidum* *L. acidophilus*		Aqueous solution	10^{6}-10^{9}	viable	30 µg/mL	79.7 90 84.3	0-80 h incubation period pH=3-9	Hussien, 2008
L. rhamnosus	GG	Aqueous solution		Treatment with: Sodium dodecyl sulphate Urea CaCl2 MgCl2 EDTA EGTA		 89 78 49 54 49 50		Lahtinen et al., 2004
B. breve *Propionibacterium freudenreichii*	Bbi99/E8 shermanii JS	aqueous solution	10^{7}-10^{8}	viable	2 g/L	21.4 12.5	1 h incubation period at 37 °C	Halttunen et al., 2008
L. plantarum	BS22	GIT of broiler chickens	1.0×10^{8}	viable	50 µg/kg	50	28 days incubation period	Zeng et al., 2018
L. brevis *L. casei* *L. lactis* *L. lactis* *L. plantarum* *L. plantarum* *L. rhamnosus* *L. rhamnosus* *L. rhamnosus* *L. rhamnosus*	Lb1 Lc12 Lb5 Lb8 Lb7 Lb9 Lb44 Lb21 Lb31 Lb103	Liquid media		viable	10 µg/mL	4.46 22.28 16.81 20.26 2.14 5.21 25.27 23.01 31.12 30.77	48 h incubation period at 30 °C pH=6.5	Zinedine et al., 2005

L. rhamnosus *Leuconostoc mesenteroides* *Pediococcus acidilactici*	Lb50 Ln13 P5					44.89 2.15 1.80		
L. rhamnosus	GG	aqueous solution	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	66 72 85	Treatment with Pronase E	Haskard et al., 2000
L. rhamnosus	GG	aqueous solution	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	76 74 89	Treatment with Lipase	Haskard et al., 2000
L. rhamnosus	GG	Phosphate buffer	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	86 85 91		Haskard et al., 2000
L. rhamnosus	GG	aqueous solution	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	60 49 36	Treatment with Periodate	Haskard et al., 2000
L. rhamnosus	GG	aqueous solution	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	83 84 80	Treatment with Iodate	Haskard et al., 2000
L. rhamnosus	GG	aqueous solution	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	64 60 50	Treatment with Urea (8 M)	Haskard et al., 2000
L. rhamnosus	GG	water	1×10^{10}	Viable Heat-treated Acid-treated	5 µg/mL	76 83 84		Haskard et al., 2000

Legend: *L.* is abbreviation of *Lactobacillus*; *S.* is abbreviation of *Saccharomyces*; *B.* is abbreviation of *Bifidobacterium*

Table 2 Several kinds of probiotics applied for detoxification of aflatoxin M_1

probiotic	Strain	Medium kind	Probiotic concentration (CFU/mL)	Probiotic Condition	Initial AFM_1 Concentration	AFM_1 removal %	Explanation	References
L. acidophilus	LA-5	yoghurt	1×10^8	viable	0.1, 0.5, 0.75 µg/L	90	in the presence and absence of yoghurt starter	Adibpour et al., 2016
L. rhamnosus	GG	liquid media	5×10^8 - 10^{10}	Viable and heat treated	50, 100 µg/L	63	18 h incubation period at 37 °C Partial reversible	Assaf et al., 2018
S. cerevisiae		yoghurt	2.1×10^9	viable, acid-, heat- and ultrasound-treated	100, 500 and 750 pg/ mL	74.2- 76.4	different storage times (1, 7, 14 and 21 days)	Karazhiyan et al., 2016
L. plantarum	MON03	liquid medium	1×10^9	viable	100 mg/kg	93	24 h incubation period	Ben Salah-Abbe`s et al., 2015
L. bulgaricus		yogurt	1×10^6	viable	50 µg/L	58.5	14 h incubation period at 37 °C	El Khoury et al., 2011
Streptococcus thermophilus						37.7		
L. acidophilus	LA1	milk		Viable		18.3		Pierides et al., 2000
				Heat killed		25.5		
L. delbrueckii subsp.		Milk				27.6	4 h incubation period at 37 °C	Sarimehmetoglu & Küplülü, 2004
Bulgaricus	ST-36	PBS				18.7	pH dependent	
Streptococcus		Milk				39.16		
thermophilus		PBS				29.42		
L. gasseri		milk		Viable		30.8		Pierides et al., 2000
				Heat killed		61.5		
L. rhamnosus	LC705			Heat killed		50		
L. lactis	cremoris			Viable		40.4		
L. lactis	ARH74			Heat killed		38.9		
L. acidophilus	NRRL B-	milk		viable	10 ng/mL	22.72	37 °C	Serrano-Niño et al., 2013
L. reuteri	4495					26.5		
L. rhamnosus	NRRL B-					24.54		
L. johnsonii	14171					32.2		
B. bifidum	NRRL					45.17		

Legend: *L.* is abbreviation of *Lactobacillus*; *S.* is abbreviation of *Saccharomyces; B.* is abbreviation of *Bifidobacterium*.

Aflatoxin removal mainly relies on aflatoxin binding to probiotic cell walls rather than bacterial metabolism. This removal was described as a reversible phenomenon, probiotic strain- and dose-dependent, and did not affect the viability of probiotics. Binding is related to some protein and carbohydrate components in the cell wall of probiotics. The stability and strength of binding of probiotics to aflatoxins is also a key consideration for evaluation of probiotic strains ability to decline aflatoxins. The binding stability depends on the environmental conditions (such as pH), probiotic strain, amino acid composition of peptidoglycan structure, formation medium conditions and the treatment used to investigate stability. According to previous studies, aflatoxin binding could be permanent if the probiotic strains are dead, whereas the living probiotics may release some of the aflatoxin content with time. As reported, treated probiotic cells with physical and chemical treatments (high temperature, adding metal ions or acids, alkaline and enzymatic treatments) seems to increase their aflatoxin binding efficiency due to the impact of hydrophobic and electrostatic interactions. This is quite related to the probiotic cell wall components, mainly peptidoglycans and exopolysaccharides. Even though probiotic effect can be varied between species and strains of probiotics, the most efficient probiotic strains could be applied as biological detoxifying agents in various kinds of food and livestock feed frequently contaminated by aflatoxins in order to increase food safety.

As reported by several researches, under appropriate *in vitro* conditions, *L. rhamnosus* and *L. bulgaricus* have high potential for removal of AFB_1 and AFM_1, respectively. *In vivo* studies are all in agreement that aflatoxin binding by probiotics is in fact better at lower pH, therefore, the probiotics have the ability to bind with aflatoxins in the small intestine and subsequently preventing toxicity of aflatoxin. Despite the promising research findings, future studies should also focus on the potential release of aflatoxins (from probiotics) after ingestion and the dose of toxicity of the bound aflatoxin compared to its unbound form.

Until now, all the studies have been conducted bench scale and there are not any applicable industrial reports for probiotics application in detoxification of aflatoxins from foods. So, further research on the pilot and industrial scale of such process is required. Also, future study on screening of new probiotic strains, combination of different probiotic strains, improvement of culture conditions, genetic engineering, and modeling of bioprocess would be required in this field of research.

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REFERENCES

ADIBPOUR, N., SOLEIMANIAN-ZAD, S., SARABI-JAMAB, M., TAJALLI, F. 2016. Effect of storage time and concentration of aflatoxin M1 on toxin binding capacity of *L. acidophilus* in fermented milk product. *Journal* of *Agricultural Science* and *Technology*, 18, 1209-1220.

AHLBERG, S.H., JOUTSJOKI, V., KORHONENA, H.J. 2015. Potential of lactic acid bacteria in aflatoxin risk mitigation. *International Journal of Food Microbiology*, 207, 87-102. http://dx.doi.org/10.1016/j.ijfoodmicro.2015.04.042

AMBROSINI, V.M., GONZALEZ, S., PERDIGON, G., DE RUIZ HOLDAGO, A.P., OLIVER, G. 1996. Chemical composition of the cell wall of lactic acid bacteria and related species. *Chemical and Pharmaceutical Bulletin*, 44 (11), 2263-2267.

ARMANDO, M., PIZZOLITTO, R., DOGI, C., CRISTOFOLINI, A., MERKIS, C., POLONI, V. 2012. Adsorption of ochratoxin A and zearalenone by potential probiotic *Saccharomyces cerevisiae* strains and its relation with cell wall thickness. *Journal of Applied Microbiology*, 113, 256-264. http://dx.doi.org/10.1111/j.1365-2672.2012.05331.x

ASSAF, J.C., ATOUI, A., EL KHOURY, A., CHOKR, A., LOUKA, N. 2018. A comparative study of procedures for binding of aflatoxin M1 to *Lactobacillus rhamnosus* GG. *Brazilian Journal of Microbiology*, 49, 120-127. http://dx.doi.org/10.1016/j.bjm.2017.05.003

BAPTISTA, A.S., HORII, J., CALORI-DOMINGUES, M.A., DA GLORIA, E.M., SALGADO, J.M., VIZIOLI, M.R. 2004. The capacity of mannooligosaccharides thermolysed yeast and active yeast to attenuate aflatoxicosis. *World Journal of Microbiology and Biotechnology*, 20(5), 475-481.

BEJAOUI, H., MATHIEU, F., TAILLANDIER, P., LEBRIHI, A. 2004. Ochratoxin A removal in synthetic and natural grape juices by selected oenological *Saccharomyces* strains. *Journal of Applied Microbiology*, 97(5), 1038-1044. http://dx.doi.org/10.1111/j.1365-2672.2004.02385.x

BEN SALAH-ABBE`S, J.B., ABBE`S, S., JEBALI, R., HAOUS, Z., OUESLATI, R. 2015. Potential preventive role of lactic acid bacteria against aflatoxin M1 immunotoxicity and genotoxicity in mice. *Journal of Immunotoxicology*, 12(2), 107-114. http://dx.doi.org/10.3109/1547691X.2014.904025

BEVILACQUA, A., PETRUZZI, L., CORBO, M.R., BAIANO, A., GAROFALO, C., SINIGAGLIA, M. 2014. Ochratoxin A released back into the medium by *Saccharomyces cerevisiae* as a function of the strain, washing medium and fermentative conditions. *Journal of the Science of Food and Agriculture*, 94, 3291-3295. http://dx.doi.org/10.1002/jsfa.6683

BOVO, F., CORASSIN, C.H., ROSIM, R.E., OLIVEIRA, C.A.F. 2012. Efficiency of lactic acid bacteria strains for decontamination of aflatoxin M1 in phosphate buffer saline solution and in skim milk. *Food and Bioprocess Technology*, 5(1), 1-5.

BOVO, F., FRANCO, L.T., ROSIM, R., FAVARO, E., TRINDADE, C.S., FERNANDES DE OLIVEIRA, C.A. 2014. The ability of *Lactobacillus rhamnosus* in solution, spray-dried or lyophilized to bind aflatoxin B1. *Journal of Food Researches*, 3, 35-41. http://dx.doi.org/10.5539/jfr.v3n2p35

BUENO, D.J., CASALE, C.H., PIZZOLITTO, R.P., SALANO, M.A., OLIVIER, G. 2006. Physical adsorption of Aflatoxin B1 by lactic acid bacteria and *Saccharomyces cerevisiae*: A theoretical model. *Journal of Food Protection*, 70(9), 2148-2154.

CHAPOT-CHARTIER, M., KULAKAUSKAS, S. 2014. Cell wall structure and function in lactic acid bacteria. *Microbial Cell Factories*, 13, S9. https://doi.org/10.1186/1475-2859-13-S1-S9

COALLIER-ASCAH, J., IDZIAK, E.S. 1985. Interaction between *Streptococcus lactis* and *Aspergillus flavus* on production of aflatoxin. *Applied Environmental Microbiology*, 49(1), 163-167.

CORASSIN, C.H., BOVO, F., ROSIM, R.E., OLIVEIRA, C.A.F. 2013. Efficiency of *Saccharomyces cerevisiae* and lactic acid bacteria strains to bind aflatoxin M-1 in UHT skim milk. *Food Control*, 31, 80-83. https://doi.org/10.1016/j.foodcont.2012.09.033

DALIÉ, D.K.D., DESCHAMPS, A.M., RICHARD-FORGET, F. 2010. Lactic acid bacteria – Potential for control of mould growth and mycotoxins: A review. *Food Control*, 21, 370-380. https://doi.org/10.1016/j.foodcont.2009.07.011

DAMAYANTI, E., ISTIQOMAH, L., SARAGIH, J.E., PURWOKO, T., SARDJONO, E. 2017. Characterization of lactic acid bacteria as poultry probiotic candidates with aflatoxin B1 binding activities. *Environmental Earth* Sciences, 101, 1-8.

EL KHOURY, A., ATOUI, A., YAGHI, J. 2011. Analysis of aflatoxin M1 in milk and yogurt and AFM1 reduction by lactic acid bacteria used in Lebanese industry. *Food Control*, 22, 1695-1699. https://doi.org/10.1016/j.foodcont.2011.04.001

ELGERBI, A.M., AIDOO, K.E., CANDLISH, A.A.G., WILLIAMS, A.G. 2006. Effects of lactic acid bacteria and bifidobacteria on levels of aflatoxin M1 in milk and phosphate buffer. *Milchwissenschaft*, 61(2), 197-199.

EL-NEZAMI, H.S., POLYCHRONAKI, N.N., MA, J., ZHU, H., LING, W., SALMINEN, E.K. 2006. Probiotic supplementation reduces a biomarker for increased risk of liver cancer in young men from Southern China. *American Journal of Clinical Nutrition*, 83, 1199-1203. http://dx.doi.org/10.1093/ajcn/83.5.1199

EL-NEZAMI, H., KANKAANPAA, P., SALMINEN, S., AHOKAS, J. 1998. Ability of dairy strains of lactic acid bacteria to bind a common food carcinogen, aflatoxin B1. *Food and Chemical Toxicology*, 36, 321-326.

EL-NEZAMI, H., MYKKANEN, H., KANKAANPAA, P., SALMINEN, S., AHOKAS, J. 2000. Ability of *Lactobacillus* and *Propionibacterium* strains to remove aflatoxin B1, from the chicken duodenum. *Journal of Food Protection*, 63, 549-552.

EL-NEZAMI, H., POLYCHRONAKI, N., SALMINEN, S., MYKKANEN, H. 2002. Binding rather than metabolism may explain the interaction of two food-grade *Lactobacillus* strains with zearalenone and its derivative alpha-zearalenol. *Applied Environmental Microbiology*, 68(7), 3545-3549. http://dx.doi.org/10.1128/aem.68.7.3545-3549.2002

ELSANHOTY, R.M., AL-TURKI, I.A., RAMADAN, M.F. 2016. Application of lactic acid bacteria in removing heavy metals and aflatoxin B1 from contaminated water. *Water Science and Technology*, 74 (3), 625-638. https://doi.org/10.2166/wst.2016.255

ELSANHOTY, R.M., SALAM, S.A., RAMADAN, M.F., BADR, F.H. 2014. Detoxification of aflatoxin M1 in yoghurt using probiotics and lactic acid bacteria. *Food Control*, 43, 129-134. https://doi.org/10.1016/j.foodcont.2014.03.002

EUROPEAN COMMISSION. 2006. Commission Regulation (EC) No.1881/2006 of 19 December. Setting maximum levels for certain contaminants in foodstuffs. *Official Journal of the European Union*, 364, 5-24.

FAZELI, M.R., HAJIMOHAMMADALI, M., MOSHKANI, A., SAMADI, N., JAMALIFAR, H., KHOSHAYAND, M.R. 2009. Aflatoxin B1 binding capacity of autochthonous strains of lactic acid bacteria. *Journal of Food Protection*, 72, 189-192.

FERNANDEZ JURI, M.G., DALCERO, A.M., MAGNOLI, C.E. 2014. *In vitro* aflatoxin B1 binding capacity by two *Enterococcus faecium* strains isolated from healthy dog faeces. *Journal of Applied Microbiology*, 118, 574-582. http://dx.doi.org/10.1111/jam.12726

FOCHESATO, A.S., CUELLO, D., POLONI, V., GALVAGNO, M.A., DOGI, C.A., CAVAGLIERI, L.R. 2018. Aflatoxin B1 adsorption/desorption dynamics in the presence of *Lactobacillus rhamnosus* RC007 in a gastrointestinal tract-simulated model. *Journal of Applied Microbiology*, 126, 223-229. http://dx.doi.org/10.1111/jam.14101

FOOD AND AGRICULTURE ORGANIZATION (FAO). 2016. Probiotics in animal nutrition – production, impact and regulation by YADAV, S., BAJAGAI ATHOL, V., KLIEVE PETER, J., WAYNE, L. p. 179.

FOOD AND DRUG ADMINISTRATION (FDA). 2005. Compliance ProgramGuidance Manual. Accessed 31.03.16.
GHOFRANI TABARI, D., KERMANSHAHI, H., GOLIAN, A., MAJIDZADEH HERAVI, R. 2018. *In Vitro* binding potentials of Bentonite, yeast cell wall and lactic acid bacteria for aflatoxin B1 and Ochratoxin A. *Iranian Journal of Toxicology*, 12(2), 7-13. http://dx.doi.org/10.29252/arakmu.12.2.7
GONZALEZ PEREYRA, M.L., MARTINEZ, M.P., CAVAGLIERI, L.R. 2018. Antifungal and aflatoxin-reducing activity of extracellular compounds produced by soil *Bacillus* spp. with potential application in agriculture. *Food Control*, 85, 392-399. http://dx.doi.org/10.1016/j.foodcont.2017.10.020
GOURAMA, H., BULLERMAN, L.B. 1997. Anti-aflatoxigenic activity of *Lactobacillus casei pseudoplantarum*. *International Journal of Food Microbiology*, 34(2), 131-143.
GRATZ, S.W., MYKKANEN, H., EL-NEZAMI, H.S. 2010. Probiotics and gut health: a special focus on liver diseases. *World Journal of Gastroenterology*, 16, 403-409. http://dx.doi.org/10.3748/wjg.v16.i4.403
GRATZ, S., MYKKÄNEN, H., ELNEZAMI, H. 2005. Aflatoxin B1 binding by a mixture of *Lactobacillus* and *Propionibacterium*: *In vitro* versus *ex vivo*. *Journal of Food Protection*, 68, 2470-2474.
GRATZ, S., MYKKÄNEN, H., OUWEHAND, A.C., JUVONEN, R., SALMINEN, S., EL-NEZAMI, H. 2004. Intestinal mucus alters the ability of probiotic bacteria to bind aflatoxin B1 *in vitro*. *Applied Environmental Microbiology*, 70, 6306-6308. http://dx.doi.org/10.1128/AEM.70.10.6306-6308
GRATZ, S., TÄUBEL, M., JUVONEN, R.O., VILUKSELA, M., TURNER, P.C., MYKKÄNEN, H. 2006. *Lactobacillus rhamnosus* strain GG modulates intestinal absorption, fecal excretion, and toxicity of aflatoxin B1 in rats. *Applied Environmental Microbiology*, 72 (11), 7398-7400. http://dx.doi.org/10.1128/AEM.01348-06
GRATZ, S., WU, Q.K., EL-NEZAMI, H., JUVONEN, R.O., MYKKANEN, H., TURNER, P.C. 2007. *Lactobacillus rhamnosus* strain GG reduces aflatoxin B1 transport, metabolism, and toxicity in Caco-2 cells. *Applied Environmental Microbiology*, 73(12), 3958-3964. http://dx.doi.org/10.1128/AEM.02944-06
GRENIER, B., APPLEGATE, T.J. 2013. Modulation of intestinal functions following mycotoxin ingestion: meta-analysis of published experiments in animals. *Toxins*, 5, 396- 430. http://dx.doi.org/10.3390/toxins5020396
GROHS, R., VSETECKA, S., WAGNER, U. 2004. Assessing the Effectiveness of Sport Sponsorships: An Empirical Examination. *Schmalenbach Business Reviews*, 56, 119-138. http://dx.doi.org/10.1007/BF03396689
HADIANI, M.R., KHOSRAVI-DARANI, K., RAHIMIFARD, N., YOUNESI, H. 2018a. Assessment of Mercury biosorption by *Saccharomyces cerevisiae*: Response surface methodology for optimization of low Hg (II) concentrations. *Journal of Environmental Chemical Engineering*, 6(4), 4980-4987. https://doi.org/10.1016/j.jece.2018.07.034
HADIANI, M.R., KHOSRAVI-DARANI, K., RAHIMIFARD, N., YOUNESI, H. 2018b. Biosorption of low concentration levels of Lead (II) and Cadmium (II) from aqueous solution by *Saccharomyces cerevisiae*: Response surface methodology. *Biocatalysis* and *Agricultural Biotechnology*, 15, 25-34. https://doi.org/10.1016/j.bcab.2018.05.001
HALTTUNEN, T., COLLADO, M.C., EL-NEZAMI, H., MERILUATO, J., SALMINEN, S. 2008. Combining strains of lactic acid bacteria may reduce their toxin and heavy metal removal efficiency from aqueous solution. *Letters in Applied Microbiology*, 46, 160-165. http://dx.doi.org/10.1111/j.1472-765X.2007.02276.x
HAMIDI, A., MIRNEJAD, R., YAHAGHI, E., BEHNOD, V., MIRHOSSEINI, A., AMANI, S. 2013. The aflatoxin B1 isolating potential of two lactic acid bacteria. *Asian Pacific Journal of Tropical Biomedicine*, 3, 732-736. http://dx.doi.org/10.1016/S2221-1691(13)60147-1
HASKARD, C.A., EL-NEZAMI, H.S., KANKAANPÄÄ, P.E., SALMINEN, S., AHOKAS, J.T. 2001. Surface binding of aflatoxin B1 by lactic acid bacteria. *Applied* and *Environmental Microbiology*, 67, 3086-3091. http://dx.doi.org/10.1128/AEM.67.7.3086-3091.2001
HASKARD, C., BINNION, C., AHOKAS, J. 2000. Factors affecting the sequestration of aflatoxin by *Lactobacillus rhamnosus* strain GG. *Chemico-Biological Interactions*, 128, 39-49.
HATHOUT, A.S., MOHAMED, S.R., EL-NEKEETY, A.A., HASSAN, N.S., ALY, S.E., ABDEL-WAHHAB, M.A. 2011. Ability of *Lactobacillus casei* and *Lactobacillus reuteri* to protect against oxidative stress in rats fed aflatoxins-contaminated diet. *Toxicon*, 58, 179-186. http://dx.doi.org/10.1016/j.toxicon.2011.05.015
HEGAZY, E.M., SADEK, Z.I., EL-SHAFEI, K., ABD EL-KHALEK, A.B. 2011. Aflatoxins binding by *Saccharomyces cerevisiae* and *S. boulardii* in functional cereal based icecream. *Life Sciences Journal*, 8(4), 75-81.
HERNANDEZ-MENDOZA, A., GARCIA, H.S., STEELE, J.L. 2009. Screening of *Lactobacillus casei* strains for their ability to bind aflatoxin B1. *Food and Chemical Toxicology*, 47(6), 1064-1068.
HERNANDEZ-MENDOZA, A., GUZMAN-DE-PEÑA, D., VALLEJO-CÓRDOBA, B., GARCIA, H.S. 2010. *In vivo* assessment of the potential protective effect of *Lactobacillus casei* Shirota against aflatoxin B 1. *Dairy Science and Technology*, 90, 729-740. http://dx.doi.org/10.1051/dst/2010030
HUSSIEN, A.H. 2008. Effect of certain factors on surface binding of aflatoxin B1 by some probiotic strains. *Journal of Radiation Research and Applied Sciences*, 1(2), 245-250.
IHA, M.H., BARBOSA, C.B., OKADA, I.A., TRUCKSESS, M.W. 2013. Aflatoxin M1 in milk and distribution and stability of aflatoxin M1 during production and storage of yoghurt and cheese. *Food Control*, 29(1), 1-6. https://doi.org/10.1016/j.foodcont.2012.05.058
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). 2016. Agents Classified by the IARC Monographs. vol. 1–116 Available from:. http://monographs.iarc.fr/ENG/ Classification/ latest_classif. Php.
JAKHAR, K.K., SADANA, J.R. 2004. Sequential pathology of experimental aflatoxicosis in quail and the effect of selenium supplementation in modifying the disease process. *Mycopathology*, 157, 99-109.
JIANG, M., PENG, X., FANG, J., CUI, H., YU, Z., CHEN, Z. 2015. Effects of aflatoxin B1 on T-cell subsets and mRNA expression of cytokines in the intestine of broilers. *International Journal of Molecular Sciences*, 16, 6945-6959. http://dx.doi.org/10.3390/ijms16046945
KANKAANPAA, P., TUOMOLA, E., EL-NEZAMI, H.S., AHOKAS, J., SALMANIEN, S.J. 2000. Binding of aflatoxin B1 alters the adhesion properties of *Lactobacillus rhamnosus* strain GG in a Caco-2 model. *Journal of Food Protection*, 63(3), 412-414.
KARAZHIYAN, H., MEHRABAN SANGATASH, M., KARAZHYAN, R., MEHRZAD, A., HAGHIGHI, E. 2016. Ability of different treatments of *Saccharomyces cerevisiae* to surface bind aflatoxin M1 in yoghurt. *Journal of Agricultural Science and Technology*, 18, 1489-1498.
KHANAFARI, A., SOUDI, H., MIRABOULFATHI, M., OSBOO, R.K. 2007. An in vitro investigation of aflatoxin B1 biological control by *Lactobacillus plantarum*. *Pakistan Journal of Biological Sciences*, 10, 2553-2556.
LAHTINEN, S.J., HASKARD, C.A., OUWEHAND, A.C., SALMINEN, S., AHOKAS, J. 2004. Binding of aflatoxin B1 to cell wall components of *Lactobacillus rhamnosus* strain GG. *Food Additives and Contaminants*, 21, 158-164. http://dx.doi.org/10.1080/02652030310001639521
LEE, Y., EL-NEZAMI, H., HASKARD, C., GRATZ, S., PUONG, K., SALMINEN, S. 2003. Kinetics of adsorption and desorption of aflatoxin B1 by viable and nonviable bacteria. *Journal of Food protection*, 66, 426-430.
LIZÁRRAGA-PAULÍN, E.G., MORENO-MARTÍNEZ, E., MIRANDA-CASTRO, S.P. 2011. Aflatoxins and their impact on human and animal health: an emerging problem. In: Aflatoxins - Biochemistry and Molecular Biology (edited by R. G. Guevara-Gonzalez). p. 255-282. Rijeka, Croatia.
LIU, N., WANG, J., DENG, Q., GU, K., WANG, J. 2018. Detoxification of aflatoxin B_1 by lactic acid bacteria and hydrated sodium calcium aluminosilicate in broiler chickens. *Livestock Science*, 208, 28-32. https://doi.org/10.1016/j.livsci.2017.12.005
MARTINS, M.L., MARTINS, H.M., BERNARDO, F. 2001. Aflatoxins in spices marketed in Portugal. *Food Additives and Contaminants*, 18, 315-319. http://dx.doi.org/10.1080/02652030120041
MASSOUD, R., CRUZ, A., KHOSRAVI-DARANI, K. 2018. Ochratoxin A: From safety aspects to prevention and remediation strategies. *Current Nutrition and Food Science*, 14(1), 11-16. http://dx.doi.org/10.2174/1573401313666170517165500
MOTAMENY, R., SADEGHI, A.A., DEHGHAN-BANADAKY, M., CHAMANI, M., ABOLHASSANI, M. 2012. Effect of some acid treated bacteria on reduction of impure aflatoxin B1 in ruminant gastrointestinal model. *Journal of American Sciences*, 7, 213-217.
MOTAWEE, M.M., ABD EL-GHANY, M.A. 2011. Effect of some lactic acid bacteria strains on aflatoxins reduction in some dairy foods. Development of Higher Specific Education Programs in Egypt and the Arab World in the Light of Knowledge Era Requirements. *The 6th Arab and 3rd International Annual Scientific Conference*, Egypt.
NAZARETH, T.M., LUZ, C., TORRIJOS, R., QUILES, J.M., LUCIANO, F.B., MAÑES, J., MECA, G. 2020. Potential application of lactic acid bacteria to reduce Aflatoxin B_1 and Fumonisin B_1 occurrence on corn kernels and corn ears. *Toxins*, *12*, 21. https://doi.org/10.3390/toxins12010021
NIDERKORN, V., MORGAVI, D.P., ABOAB, B., LEMAIRE, M., BOUDRA, H. 2009. Cell wall component and mycotoxin moieties involved in the binding of fumonisin B1 and B2 by lactic acid bacteria. *Journal of Applied Microbiology*, 106(3), 977-985. http://dx.doi.org/10.1111/j.1365-2672.2008.04065.x
NIKBAKHT NASRABADI, E., JAMALUDDIN, R., ABDUL MUTALIB, M.S., KHAZA'AI, H., KHALESI, S., MOHD REDZWAN, S. 2013. Reduction of aflatoxin level in aflatoxin-induced rats by the activity of probiotic *Lactobacillus casei* strain Shirota. *Journal of Applied Microbiology*, 114, 1507-1515. http://dx.doi.org/10.1111/jam.12148
OLUWAFEMI, F., DA-SILVA, F.A. 2009. Removal of aflatoxins by viable and heat-killed *Lactobacillus* species isolated from fermented maize. *Journal of Applied Biosciences*, 16, 871-876.
OLUWAFEMI, F., KUMAR, M., BANDYOPADHYAY, R., OGUNBANWO, T., AYANWANDE, K.B. 2010. Bio-detoxification of aflatoxin B1 in artificially contaminated maize grains using lactic acid bacteria. *Toxin Reviews*, 29, 115-122. https://doi.org/10.3109/15569543.2010.512556

PELTONEN, K.D., EL-NEZAMI, H.S., SALMINEN, S.J., AHOKAS, J.T. 2000. Binding of aflatoxin B1 by probiotic bacteria. *Journal of the Science of Food and Agriculture*, 80, 1942-1945. https://doi.org/10.1002/1097-0010(200010)80

PELTONEN, K., EL-NEZAMI, H., HASKARD, C., AHOKAS, J., SALMINEN, S. 2001. Aflatoxin B1 binding by dairy strains of lactic acid bacteria and bifidobacteria. *Journal of Dairy Sciences*, 84, 2152-2156. http://dx.doi.org/10.3168/jds.S0022-0302(01)74660-7

PERCZAK, A., GOLIŃSKI, P., BRYŁA, M., WAŚKIEWICZ, A. 2018. The efficiency of lactic acid bacteria against pathogenic fungi and mycotoxins. *Arch Industrial Hygiene Toxicology*, 69, 32-45. https://doi.org/10.2478/aiht-2018-69-3051

PIERIDES, M., EL-NEZAMI, H., PELTONEN, K., SALMINEN, S., AHOKAS, J. 2000. Ability of dairy strains of lactic acid bacteria to bind aflatoxin M1 in a food model. *Journal of Food Protection*, 63, 645-650.

PIZZOLITTO, R.P., SALVANO, M.A., DALCERO, M. 2012. Analysis of fumonisin B1 removal by microorganisms in co-occurrence with aflatoxin B1 and the nature of the binding process. *International Journal of Food Microbiology*, 156(3), 214-221. http://dx.doi.org/10.1016/j.ijfoodmicro.2012.03.024

PRANDINI, A., TANSINI, G., SIGOLO, S., FILIPPI, L., LAPORTA, M., PIVA, G. 2009. On the occurrence of aflatoxin M1 in milk and dairy products. *Food and Chemical Toxicology*, 47, 984-991. http://dx.doi.org/10.1016/j.fct.2007.10.005

PRANOTO, Y., AMANAH, H., UTAMI, T., RAHAYU, E. 2007. Study on factors affectin aflatoxin B1 binding by *Lactobacillus acidophilus* SNP-2. *Internatinal Agriculture Engineering Conference*, Bangkok: Thailand.

RAHAIE, S., RAZAVI, S.H., EMAM JOMEH, Z. 2010. The ability of *Saccharomyces Cerevisiae* strain in aflatoxin reduction in pistachio nuts. *Iranian Journal of Food Science and Technology*, 7(1), 81-88.

RAHAYU, E.S., AMANAH, H.Z., UTAMI, R., UTAMI, T. 2007. Study on binding of AFB1 by *Lactobacillus acidophilus* SNP-2. *Asian Conference of Lactic Acid Bacteria*, Shianghai: China.

RAHNAMA VOSOUGH, P., MOHAMADI SANI, A., MEHRABAN SANGATASH, M., KARAZHYAN, R. 2013. Assessing the ability of *Lactobacillus rhamnosus* GG to bind aflatoxin B1 from contaminated cottonseed. *Biotechnology An Indian Journal*, 7(1), 28-33.

RAYES AAH. Removal of aflatoxin B1 from experimentally contaminated whole milk using a pool of probiotic strains of lactic acid bacteria and baker's yeast *Saccharomyces cerevisiae*. *New York Science Journal*, 6, 84-90.

SANDERS, M.E., LENOIR-WIJNKOOP, I., SALMINEN, S., MERENSTEIN, D.J., GIBSON, G.R., PETSCHOW, B.W. 2014. Probiotics and prebiotics: prospects for public health and nutritional recommendations. *Annals New York Academy Sciences*, 1309, 19-29. http://dx.doi.org/10.1111/nyas.12377

SANTOS, A., MARQUINA, D., LEAL, J.A., PEINADO, J.M. 2006. (1-6)-b-D-glucan as cell wall receptor for Pichia membranifaciens killer toxin. *Applied and Environmental Microbiology*, 66, 1809-1813. http://dx.doi.org/10.1128/aem.66.5.1809-1813.2000

SARIMEHMETOGLU, B., KÜPLÜLÜ, Ö. 2004. Binding ability of aflatoxin M1 to yoghurt bacteria. *Ankara University Veteriner Faculties Dergisi*, 51(3), 195-198.

SERRANO-NIÑO, J.C., CAVAZOS-GARDUÑO, A., HERNANDEZ-MENDOZA, A., APPLEGATE, B., FERRUZZI, M.G., SAN MARTIN-GONZÁLEZ, M.F. 2013. Assessment of probiotic strains ability to reduce the bioaccessibility of aflatoxin M1 in artificially contaminated milk using an in vitro digestive model. *Food Control*, 31(1), 202-207. https://doi.org/10.1016/j.foodcont.2012.09.023

SEZER, C., GÜVEN, A., BILGE ORAL, N., VATANSEVER, L. 2013. Detoxification of aflatoxin B1 by bacteriocins and bacteriocinogenic lactic acid bacteria. *Turkish Journal of Veterinary and Animal Sciences*, 37, 594-601.

SHAHIN, A.A.M. 2007. Removal of aflatoxin B1 from contaminated liquid media by dairy lactic acid bacteria. *International Journal of Agriculture and Biology*, 9(1), 71-75.

SHETTY, P.H., JESPERSEN, L. 2006. *Saccharomyces cerevisiae* and lactic acid bacteria as potential mycotoxin decontaminating agents. *Trends in Food Science and Technology*, 17(1), 48-55. https://doi.org/10.1016/j.tifs.2005.10.004

SHETTY, P.H., HALD, B., JESPERSEN, L. 2007. Surface binding of aflatoxin B1 by *Saccharomyces cerevisiae* strains with potential decontaminating abilities in indigenous fermented foods. *International Journal of Food Microbiology*, 113(1), 41-46. http://dx.doi.org/10.1016/j.ijfoodmicro.2006.07.013

SLIZEWSKA, K., NOWAK, A., LIBUDZISZ, Z., BLASIAK, J. 2010. Probiotic preparation reduces the faecal water genotoxicity in chickens fed with aflatoxin B1 contaminated fodder. *Research in Veterinary Science*, 89(3), 391-395. http://dx.doi.org/10.1016/j.rvsc.2010.04.004

SMILEY, R., DRAUGHON, F. 2000. Preliminary evidence that degradation of aflatoxin B1 by *Flavobacterium aurantiacum* is enzymatic. *Journal of Food Protection*, 63, 415-418.

TAHEUR, F.B., FEDHILA, K., CHAIEB, K., KOUIDHI, B., BAKHROUF, A,. ABRUNHOSA, L. 2017. Adsorption of aflatoxin B1, zearalenone and ochratoxin A by microorganisms isolated from Kefir grains. *International Journal of Food Microbiology*, 251, 1-7. http://dx.doi.org/10.1016/j.ijfoodmicro.2017.03.021

TOPCU, A., BULAT, T., WISHAH, R., BOYACI, I.H. 2010. Detoxification of aflatoxin B1 and patulin by *Entrococcus faecium* strains. *International Journal of Food Microbiology*, 139, 202-205. http://dx.doi.org/10.1016/j.ijfoodmicro.2010.03.006

VINDEROLA, G., RITIENI, A. 2015. Role of probiotics against mycotoxins and their deleterious effects. *Journal of Food Research*, 4, 10-21. http://dx.doi.org/10.5539/jfr.v4n1p10

WAN, M.L., TURNER, P.C., ALLEN, K.J., EL-NEZAMI, H. 2016. *Lactobacillus rhamnosus* GG modulates intestinal mucosal barrier and inflammation in mice following combined dietary exposure to deoxynivalenol and zearalenone. *Journal of Functional Foods*, 22, 34-43. https://doi.org/10.1016/j.jff.2016.01.014

YADAV, A.K., TYAGI, A., KAUSHIK, J.K., SAKLANI, A.C., GROVER, S., BATISH, V.K. 2013. Role of surface layer collagen binding protein from indigenous *Lactobacillus plantarum* 91 in adhesion and its anti-adhesion potential against gut pathogen. *Microbiological Research*, 168, 639-645. http://dx.doi.org/10.1016/j.micres.2013.05.003

YIANNIKOURIS, A., ANDRÉ, G., POUGHON, L. 2006. Chemical and conformational study of the interactions involved in mycotoxin complexation with beta-d-glucans. *Biomacromolecular Journal*, 7(4), 1147-1155. https://doi.org/10.1021/bm050968t

YU, B., CHANG, C.H., LEE, T.T. 2015. Effects of the probiotics supplementation in diet on intestinal microflora ecosystem in broilers. *Journal of Advanced Agricultural Technologies*, 2, 138-142. http://dx.doi.org/10.12720/joaat.2.2.138-142

ZENG, Y., ZENG, D., ZHANG, Y., NI, X.Q., WANG, J., JIAN, P. 2018. *Lactobacillus plantarum* BS22 promotes gut microbial homeostasis in broiler chickens exposed to aflatoxin B1. *Journal of Animal Physiology and Animal Nutrition*, 102, 449-459. http://dx.doi.org/10.1111/jpn.12766

ZINEDINE, A., FAID, M., BENLEMLIH, M. 2005. *In vitro* reduction of aflatoxin B1 by strains of lactic acid bacteria isolated from Moroccan sourdough bread. *International Journal of Agriculture and Biology*, 7, 67-70.

ZOGHI, A., KHOSRAVI-DARANI, K., SOHRABVANDI, S. 2014. Surface binding of toxins and heavy metals by probiotics. *Mini Reviews in Medicinal Chemistry*, 14, 84-98.

ZOGHI, A., KHOSRAVI-DARNI, K., SOHRABVANDI, S. 2019. Patulin removal from synbiotic apple juice using *Lactobacillus plantarum* ATCC 8014. *Journal of Applied Microbiology*, 126, 1149-1160. http://dx.doi.org/10.1111/jam.14172

ZOGHI, A., KHOSRAVI-DARANI, K., SOHRABVANDI, S., ATTAR, H., ALAVI, S. A. 2017. Effect of probiotics on patulin removal from synbiotic apple juice. *Journal of the Science of Food and Agriculture*, 97(8), 2601-2609. http://dx.doi.org/10.1002/jsfa.8082