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# Biodecontamination of milk and dairy products by probiotics: Boon for bane

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REVIEW ARTICLE

## Abstract

In recent decades, "contamination of the environment, food, and feed by different contaminants such as heavy metals and toxins is increasing due to industrial life." Commercial milk and milk products can be contaminated with heavy metals and mycotoxins. Biosorption is a low-cost method and has good potential for decontamination. In dairy products, "various starters, especially probiotics, can be used as biosorbants, while microorganisms are able to bind to heavy metals and toxins and decrease their bioavailability and hazards in the human body." In this article, the key role of dairy starters and probiotics in the decontamination of toxins and heavy metals, and the best probiotics for decontamination of aflatoxins and heavy metals has been reviewed. After a quick glance at introducing dairy products and the main risks in association with the intake of some hazardous materials from dairy products, the application of biological systems is mentioned. Then, the article is focused on the role of beneficial microorganisms as the last chance to decrease the risk of exposure to toxins and heavy metals in dairy products. This review can be helpful for biotechnologists and scientists who have challenges about the existence of heavy metals and toxins in milk and dairy products, and help them to find the best method to decrease the content of the usual contaminants.

*Keywords*: aflatoxins; biosorption; decontamination; heavy metals; dairy products

## Introduction

The World Health Organization (WHO) defines food safety as, "Approaches and methods for certifying the manufacture, maintenance, distribution and utilization of food happen in an assured system." However, some people defined safe food as food without any contamination (El Sheikha, 2015).

Heavy metals naturally exist in the environment. Industrial activities can increase their content in air and soil, leading to phytotoxicity of plants (Asati *et al.*, 2016; Yang *et al.*, 2018). Milk and dairy products have an important role in the human food chain, especially children's food; so, contamination of dairy products by toxins and heavy metals is one of the most important issues that can negatively impact consumers' health. Milk and dairy


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products can be contaminated with heavy metals under certain conditions through contamination of water and animal feed with environmental contaminants such as metal and cement smelters, sewage effluents, and industrial waste. Heavy metals' accumulation in milk can easily enter the human body and be dangerous for consumer's health (Abedi *et al.*, 2020). Dairy product contamination (heavy metal and aflatoxin) is very common all over the world (Ziarati *et al.*, 2018).

Heavy metals' toxicity occurs in levels of about 1.0–10 mg/L; however, lead and cadmium could have a toxic effect in 1–100 µg/L (Alkorta *et al.*, 2004). For example, different levels of exposure to cadmium could cause renal dysfunction, hepatic injury, and lung damage (Miura *et al.*, 2017; Naidoo *et al.*, 2019; Zhang *et al.*, 2014). Arsenic poisoning can cause death through disorder in essential metabolic enzymes (Khairul *et al.*, 2017). Maximum permissible limits of heavy metal contents in milk (considered by International Dairy Federation) are 2.6 µg/kg for cadmium, 10 µg/kg for Copper, 20 µg/kg for lead, and 328 µg/kg for zinc (Malhat *et al.*, 2012).

Aflatoxins directly (through eating contaminated food) and indirectly (primary contaminated products such as milk of contaminated livestock) can enter into the human body by the use of contaminated dairy products. Aflatoxins can cause negative effects on human health, such as liver or kidney cancer and chronic intoxications (Karazhiyan *et al.*, 2016). The most common aflatoxin in dairy products is aflatoxin $M_1$ ($AFM_1$). $AFM_1$ is a metabolite of aflatoxin $B_1$ ($AFB_1$) after ingestion of contaminated feed ($AFB_1$) by livestock. About 0.3 to 6.2% of $AFB_1$ (Abdelmotilib *et al.*, 2018) can be bio-transformed into $AFM_1$ (4-hydroxy- $AFB_1$) and can excrete into milk and urine (Iha *et al.*, 2013; Karazhiyan *et al.*, 2016). $AFM_1$ is carcinogenic and toxicogenic, and can resist pasteurization and sterilization processes (Gonçalves *et al.*, 2020). $AFM_1$ compared with $AFB_1$ is approximately 10 times less mutagenic, genotoxic, and toxigenic. Its carcinogenic effects are displayed in different kinds of species (Elsanhoty *et al.*, 2014). $AFM_1$ can also cause gene mutation, DNA damage, cell transformation in mammalian cells, and chromosomal anomalies. Food and Drug Administration (FDA) and the European Commission recommended that the maximum permissible limits of $AFM_1$ in milk are 0.5 µg/kg and 0.05 µg/kg, respectively (Commission, 2006; FDA, 2019)

It is reported that mycotoxins in milk and dairy products, which can be produced by different kinds of fungi are: Aflatoxins (by *Aspergillus*), Compactin (by *Penicillium*), Cyclopaldic acid (by *Penicillium*), and Patulin (by *Penicillium*) (El Sheikha, 2019).

Many reports have investigated regarding contamination of milk by heavy metals and toxins all over the world. According to Tables 1 and 2, which present some of the above reports, the amount of lead in Iraq, Brazil, China, Spain, and Italy was more than the maximum permissible

**Table 1. Some important data about milk contamination to heavy metals (from 2014 to 2021).**

| Country | Contamination | Concentration | Reference |
|---|---|---|---|
| Egypt | Pb<br>Cd | 0.044–0.751 mg/L<br>0.008–0.179 mg/L | Meshref *et al.*, 2014 |
| Serbia | Pb<br>Cd | 54.3–95.2 lg/kg<br>2.13–4.82 lg/kg | Suturović *et al.*, 2014 |
| Iraq | Pb | 32 µg/L | Alani and Al-Azzawi, 2015 |
| Pakistan | Pb<br>Cd | 0.014 mg/Kg<br>0.001 mg/Kg | Ismail *et al.*, 2015 |
| Bangladesh | Pb<br>Cd | 0.2 mg/L<br>0.073 mg/L | Muhib *et al.*, 2016 |
| Iran | Pb<br>Cd | 14.0 µg/kg<br>1.11 µg/kg | Shahbazi *et al.*, 2016 |
| Brazil | Pb | 2.12–37.36µg/L | de Oliveira *et al.*, 2017 |
| Mexico | Pb<br>As | 0.03 mg/Kg<br>0.12 mg/Kg | Castro-González *et al.*, 2018 |
| Poland | Pb<br>Cd | 5.24 µg/L<br>0.15 µg/L | Halagarda *et al.*, 2018 |
| Turkey | Pb<br>Cd<br>As | 0.0055 mg/L<br>0.088 mg/L<br>0.002 mg/L | Seğmenoğlu and Baydan, 2021 |

As: Arsenic, Cd: Cadmium, Pb: Lead

**Table 2. Some important data about milk contamination to mycotoxins in world from 2014 to 2021.**

| Country | Contamination | Concentration | Reference |
|---|---|---|---|
| Croatia | $AFM_1$ | 0.003–1.135 µg/L | Bilandžić *et al.*, 2014 |
| China | $AFM_1$<br>OA<br>ZEA<br>α-ZEA | 80.4 ng/kg<br>56.7 ng/kg<br>14.9 ng/kg<br>24.3 ng/kg | Huang *et al.*, 2014 |
| Serbia | $AFM_1$ | 0.01–1.2 µg/kg | Kos *et al.*, 2014 |
| Iran | $AFM_1$ | > 0.05 µg/L | Fallah *et al.*, 2015 |
| Macedonia | $AFM_1$ | 408.1 ng/L | Dimitrieska-Stojković *et al.*, 2016 |
| Pakistan | $AFM_1$ | >2610 ng/L | Aslam *et al.*, 2016 |
| Argentina | $AFM_1$ | 293 ng/L | Michlig *et al.*, 2016 |
| Bosnia and Herzegovina | $AFM_1$ | 60 ng/L | Bilandžić *et al.*, 2016 |
| Italy | $AFM_1$ | 52 ng/L | De Roma *et al.*, 2017 |
| Tanzania | $AFM_1$ | 0.627 ng/mL | Karczmarczyk *et al.*, 2017 |
| Malaysia | $AFM_1$ | 144 ng/L | Shuib *et al.*, 2017 |
| Kosovo | $AFM_1$ | 83 ng/L | Camaj *et al.*, 2018 |
| El Salvador | $AFM_1$ | Approximately 100 ng/L | Peña-Rodas *et al.*, 2018 |
| Turkey | $AFM_1$ | 78.69 ng/L | Eker *et al.*, 2019 |
| Ethiopia | $AFM_1$ | 207 ng/L | Zakaria *et al.*, 2019 |
| Kenya | $AFM_1$ | 4563 ng/L | Kuboka *et al.*, 2019 |
| Brazil | $AFM_1$ | 45.18 ng/L | Venâncio *et al.*, 2019 |
| Ecuador | $AFM_1$ | 0.0774 µg/kg | Puga-Torres *et al.*, 2020 |
| Spain | $AFM_1$ | 0.009–1.36 µg/kg | Rodríguez-Blanco *et al.*, 2020 |
| India | $AFM_1$ | 1116 ng/L | Sharma *et al.*, 2020 |
| Morocco | $AFM_1$ | 4.46 ± 14.09 ng/L | Mannani *et al.*, 2021 |
| Malawi | $AFM_1$ | 0.551 µg/L | Njombwa *et al.*, 2021 |
| Spain | $AFM_1$<br>$AFB_1$ | 12.6 ng/kg<br>0.61 µg/kg | Bervis *et al.*, 2021 |

$AFM_1$: Aflatoxin $M_1$, $AFB_1$: Aflatoxin $B_1$, OA: Ochratoxin A, ZEA: Zearalenone, α-ZEA: α-zearalenone.

limits. Also, $AFM_1$ in China and India, and cadmium in Poland and Spain, were higher than permissible limits. This information confirms the importance of decontamination in milk and dairy products.

There are different methods for the decontamination of dairy products, such as physical, chemical (reverse osmosis, ion exchange, freeze concentration, and evaporation) (Patterson and Minear, 2013), and biological methods (using different biomaterials such as bacteria and yeasts biomass, plants, and seaweeds) (Abdelmotilib *et al.*, 2018; Hashim and Chu, 2004; Hayat *et al.*, 2017; Satyapal *et al.*, 2016; Sulaymon *et al.*, 2013; Vishnoi *et al.*, 2014). Adsorption is one of the most important decontamination strategies in dairy products (Giovati *et al.*, 2015; Massoud *et al.*, 2019; Milanowski *et al.*, 2017; Porova *et al.*, 2014). There are different biosorbents, such as "algae, plants, yeasts, fungi, and bacteria," for the bioremoval of toxins and metals in fermented dairy products (e.g., kefir, kumis, yogurt, and doogh). Probiotic bacteria can also be used for this purpose. Fermented dairy products are very popular, and they have a perfect taste (El Sheikha *et al.*, 2018; Yerlikaya, 2014). Probiotics can reduce contamination (heavy metals and aflatoxins) in fermented dairy products (Zoghi *et al.*, 2014). They are widely used for bioremoval of toxins (Massoud *et al.*, 2018; Zoghi *et al.*, 2017, 2019) as well as heavy metals (arsenic, mercury, lead, and cadmium) (Hadiani *et al.*, 2018, 2019; Khosravi-Darani *et al.*, 2019), heterocyclic aromatic amines (Khosravi-Darani *et al.*, 2019; Sarlak, 2020), and even pesticides (Wochner *et al.*, 2018).

In this article, reports about the influence of adding starters and probiotics into the formulation of dairy products on the bioremoval of contaminations such as toxins and heavy metals are reviewed.

## Starters and Probiotics in Dairy Products

Food fermentation by microorganisms is one of the most economic and widely practiced methods for improving

texture, flavor, and functionality, and also for enhancing the shelf life of food products (Ray *et al.*, 2014; Salque *et al.*, 2013). The fermentation process can be carried out with starter cultures to certify consistency in commercial products by using familiar microorganisms with favorable traits, such as a high amount of acidification via the manufacture of lactic acid and/or the sprinkling of secondary metabolites in the product matrix (Ryan *et al.*, 2015). Different starters have been used for producing various dairy products all around the world. Some of these products and their starters are mentioned in Table 3.

**Table 3. Some fermented dairy products and related starters.**

| Fermented dairy products | Country/Region of origin | Starters | Reference |
|---|---|---|---|
| Acidophilus milk | — | *Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, Lactobacillus bulgaricus, Streptococcus thermophilus* | Raftaniamiri *et al.*, 2010 |
| Buttermilk | Egypt and Ethiopia | (cultured buttermilk) Lactic acid bacteria (e.g., *Lactococcus*, *Lactobacillus*, *Streptococcus*, and *Leuconostocs*) | El Sheikha and Montet, 2014; Kumar *et al.*, 2015 |
| Cheese | — | (cheddar cheese) Lactic acid bacteria starter culture *(Lactococcus lactis ssp. lactis, Lactococcus lactis ssp. cremoris, and Streptococcus salivarius spp. thermophilus*) | Ferreira and Viljoen, 2003 |
| Matzoon | Armenia | Lactic acid bacteria | Macori and Cotter, 2018 |
| Leben | Arab World | (Leben from camel milk) *Lactococcus lactis, Lactobacillus pentosus, Lactobacillus plantarum, Lactobacillus brevis,* and *Pediococcus pentosaceus* | Fguiri *et al.*, 2013 |
| Kishk | Arab World | Freeze-dried yogurt starter culture | Tamime *et al.*, 2000 |
| Kumis | Central Asia<br>Turkic countries<br>Central Asia | *Lactococcus lactis subsp. lactis, Streptococcus thermophilus, Lactobacillus delbrueckii subsp. bulgaricus, Lactobacillus helveticus, Lactobacillus casei subsp. Pseudoplantarum, and Lactobacillus brevis*<br>*Kluyveromyces marxianus var. lactis, Saccharomyces cerevisiae, Candida inconspicua, and Candida maris* | Simova *et al.*, 2002 |
| Ymer | Denmark | *Streptococcus lactis, Streptococcus diacetilaclis., Streptococcus cremoris, and Leuconostoc citrovorum* | Poulsen, 1970 |
| Kefir | Estonia, Hungary, Greece, Latvia, Romania, Slovakia, Bosnia and Herzegovina | *Lactobacilli*<br>*Lactococcus*<br>Acetic acid bacteria<br>and yeast | Garrote *et al.*, 2001 |
| Dahi | India | *Lactobacillus case* or *Lactobacillus acidophilus* | Yadav *et al.*, 2005 |
| Mishti doi | India | *Streptococcus salivarius ssp. Thermophiles, Lactobacillus acidophilus, Lactobacillus delbrueckii ssp. bulgaricus, Lactobacillus acidophilus, Lactococcus lactis ssp. lactis, Saccharomyces cerevisiae* | Gupta *et al.*, 2000 |
| Matsoni | Georgia | *Lactobacillus Streptococcus, Kluyveromyces marxianus, Candida famata, Saccharomyces cerevisiae, Lodderomyces elongisporus, Kluyveromyces lactis* | Bokulich *et al.*, 2015 |
| Wara | Africa | *Lactobacillus sp., Leuconostoc sp., Pediococuus sp., Lactococcus sp., yeasts* | El Sheikha and Montet, 2014 |
| Biruni | Sudan | *Lactic acid bacteria* | El Sheikha and Montet, 2014 |
| Mish | Sudan and Egypt | *Lactic acid bacteria* | El Sheikha and Montet, 2014 |
| Rob | Sudan | *Lactic acid bacteria* | El Sheikha and Montet, 2014 |
| Doogh | Iran | *Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus casei, Bifidobacterium lactis* | Sarlak *et al.*, 2017 |
| Yogurt | Serbia | *Streptococcus thermophilus and Lactobacillus bulgaricus* | Elsanhoty *et al.*, 2014 |
| Clabber | United States | Starters like Kefir | Dyomina *et al.*, 2017 |

FAO (2001) defined probiotics as, "viable microorganisms, that while ingested in sufficient amounts, exert health benefits on the host (FAO/WHO, 2001)." The main beneficial effects of probiotics on human health include mucosal immunity support, decreasing lactose intolerance, preventing respiratory infections or diarrheas, feasible hypocholesterolemia effects, prevention of intestinal pathogens, inhibition of colon cancer or inflammatory bowel disease (Sanders *et al.*, 2014; Yu *et al.*, 2015).

The application of microorganisms, especially probiotics, recently has been investigated for their potential to heavy metals and aflatoxins reduction (Zoghi *et al.*, 2014). Most species known as probiotic bacteria are *Bifidobacterium* (*B.*), *Lactobacillus* (*L.*), *Bacillus*, and yeast *Saccharomyces* (*S.*) *cerevisiae*, and some strains of *Escherichia (E.) coli*. A practical taxonomy of nonpathogenic, fermentative, and nontoxigenic probiotic bacteria is lactic acid bacteria (LAB), which are used widely in food industries (Zoghi *et al.*, 2017). LAB usually have gram-positive cell walls, and peptidoglycan is their main cell wall structural component; teichoic acid, lipoteichoic acid, some neutral polysaccharides, and a proteinous S-layer are their minor components (Zoghi *et al.*, 2014).

## Toxins' Bioremoval in Milk and Dairy Products

In recent decades, several scientific studies have been done regarding decontamination in dairy products, especially the biological decontamination method. Some of these researches are mentioned in Table 4.

El Khoury *et al*. (2011) investigated the application of LAB including *L. bulgaricus* and *Streptococcus thermophiles* on the reduction of $AFM_1$. They showed that using LAB is a potential method to decrease $AFM_1$ with the higher efficiency of *L. bulgaricus* compared to *Streptococcus thermophiles*. They also mentioned that the level of $AFM_1$, which is bound by LAB, enhanced with increasing the time of inoculation (El Khoury *et al.*, 2011). The binding ability of yogurt cultures was different. It is suggested that the difference in the binding ability of LAB is attributed to the difference in their cell-wall structure (Sarimehmetoğlu and Küplülü, 2004).

In addition to LAB, using *S. cerevisiae* is considered as an effective way for microbial detoxification (Karazhiyan et al., 2016). A systematic review by Campagnollo *et al*. (2020) focused on parameters influencing the binding process of $AFM_1$ by yeast. The overall binding level of yeast was reported as 52.05%, in which the lowest binding capacity was related to the yeast extract peptone and the highest binding was associated with the ruminal fluid. Also, different factors, including temperature, yeast, pH, and the type of aflatoxin, have been mentioned as the major parameters in the process of decontamination (Campagnollo *et al.*, 2020). Moreover, the effect of different treated *S. cerevisiae*, including heat, acid, and ultrasound treated, on the binding with $AFM_1$ was assessed by Karazhiyan *et al*. (2016). Among all treated yeasts, acid treatment had the most positive impact on yeast cells for improving their binding ability to aflatoxins which can be attributed to the release of monomers from polysaccharides under acidic conditions and their further changes into aldehydes after breaking down of glycosides linkages. After acid treatment, heat-treated yeasts showed the highest binding ability due to protein denaturation and Maillard reaction product formation, which caused an increase in the permeability of cell walls. Comparison between viable and unviable yeasts (heat, acid, and ultrasound treated) exhibited higher efficiency of unviable cells, which indicates that such treatments increase the binding capacity of yeasts (Karazhiyan *et al.*, 2016).

In a study performed by Taheur *et al*. (2017), a novel strategy for the reduction of mycotoxins using kefir grains was examined. The results showed that kefir microorganism grains could adsorb 82 to 100% of $AFB_1$, zearalenone, and ochratoxin A after cultivation in milk. The main strains that were able to adsorb mycotoxins were *L. kefiri*, *Kazachstania servazzii*, and *Acetobacter syzygii*. The *L. kefiri* KFLM3 was found to be the most active strain with an adsorption rate of 80 to 100% of the mycotoxins, and *K. servazzii* KFGY7 was found to retain higher mycotoxin than others after the desorption experiments. As a result, kefir consumption can assist in diminishing gastrointestinal absorption of mycotoxins and their toxic effects (Taheur *et al.*, 2017).

## Heavy Metals' Bioremoval in Milk and Dairy Products

In Table 5, investigations regarding heavy metal bioremoval in milk and dairy products are illustrated.

In two different studies by Massoud *et al.* (2019, 2020a), application of *S. cerevisiae* to reduce the concentrations of lead and cadmium in milk was examined. The optimization process was also performed considering three factors including contact time, concentrations of biomass, and initial content of heavy metals (Massoud *et al.*, 2019, 2020a). Generally, the rate of removal of heavy metals increased with an increase in the biomass, contact time, and concentration of heavy metals. They concluded that optimized conditions for lead removal were obtained after 4 days (at the end of storage time) with the content of $22\times10^8$ CFU/mL of yeast and 70 μg/L of lead in milk (Massoud *et al.*, 2019). Similarly, the optimized process for cadmium bioremoval was achieved after 4 days with 80 μg/L of cadmium and $30\times10^8$ CFU/mL of *S. cerevisiae*

**Table 4. Aflatoxin decontamination in milk and dairy products.**

| Product | Microorganism | Removal w/w% | Contaminant | Conditions | Reference |
|---|---|---|---|---|---|
| Milk | *Lactobacillus rhamnosus* (milk whey medium) | 46.0% | $AFB_1$ | Optimal condition: 60 min in pH 3.0 | Bovo *et al.*, 2014 |
| Milk | Kefir starters 1. *L. acidophilus*, *Bifidobacterium*, & *Streptococcus thermophiles* (*thermophilic lactic* culture) 2. *Lactococcus lactis subsp. cremoris, Leuconostoc*, *Lactococcus lactis subsp. lactis biovar diacetylactis, Lactococcus lactis, subsp. lactis,* 3. *Debaryomyces hansenii, Kluyveromyces marxianus subsp. marxianus.*, yeast pool, Lactic acid bacteria pool | Full kefir starters 11.67–34.66% Yeast pool 65.33–68.89% LAB pool 65% | $AFM_1$ | Toxin Concentration: 150, 200, and 250 ng/L Temperature: 4 °C Time: 7 days | Kamyar and Movassaghghazani, 2017 |
| Milk | *Lactobacillus helveticus* | 85% | $AFM_1$ | Time: 60 min | Ismail *et al.*, 2017 |
| Milk | *Saccharomyces cerevisiae* | 81.3% | $AFM_1$ | Time: 48 h | Foroughi *et al.*, 2018 |
| Yogurt | A: *S. thermophilus* & *L. bulgaricus* B: 50% *S. thermophilus* & *L. bulgaricus* 50% *L. planetarum* C: 50% *S. thermophilus and L. bulgaricus,* 50% *L. acidophilus* | Treatment B: Highest reduction 31.5–87.8% | $AFM_1$ | Temperature: 5°C, Storage time: 1, 3, 5, and 7 days | Elsanhoty *et al.*, 2014 |
| Yoghurt | *Lactobacillus acidophilus* | 90% | $AFM_1$ | $10^8$ CFU/ mL, Initial concentration of $AFM_1$:0.1, 0.5, 0.75 µg/L | Adibpour *et al.*, 2016 |
| Yoghurt | *Saccharomyces cerevisiae* | 76.46% | $AFM_1$ | Aflatoxin $M_1$: 100, 500, and 750 g/ $M_1$, in 1, 7, 14, and 21 days, yeast treatments: heat, acid, and ultrasound | Karazhiyan *et al.*, 2016 |
| Yoghurt | *Lactobacillus* plantarum, *Bifidobacterium animalis*, *Bifidobacterium* bifidum | Yogurt starters and *B. bifidum*, *B. animalis* (60.8%), Yogurt starters and *L. plantarum*, *B. Bifidum* 55.1%) | $AFM_1$ | Storage time: 1 or 10 days | Sevim *et al.*, 2019 |
| Yogurt | *L. plantarum, B. animalis,* & *B. bifidum, L. plantarum* | 49–60% | $AFM_1$ | Contact time: 4 h Temperature: 42°C | Sevim *et al.*, 2019 |
| Kefir | *Lactobacillus casei* & kefir starter | 88.17% | $AFM_1$ | Aflatoxin $M_1$ 500 pg, Kefir starters 2, 4, 6, 8, 10%, *L. casei:* 0.1, 0.3, 0.5, 0.7, 0.9 % in 48 h | Sani *et al.*, 2014 |
| Kefir | Kefir-grains | 96.8% | $AFG_1$ | Toxin concentration 5, 10, 15, 20, 25 ng/g, Kefir grain:5, 10, 20, 10, 25%, in 0, 2, 4, 6, 8 h, at 20, 30, 40, 50, 60°C | Ansari *et al.*, 2015 |

(*continues*)

**Table 4. Continued**

| Product | Microorganism | Removal w/w% | Contaminant | Conditions | Reference |
|---|---|---|---|---|---|
| Kefir | Kefir grains: *Lactobacillus kefiri, Kazachstania servazzii, Acetobacter syzygii* | 82–100% | $AFB_1$, ZEA, OA | 1 µg/Ml mycotoxin, Kefir grains 10% w/v in 24 at 25°C | Taheur *et al.*, 2017 |
| UHT skim milk | Lactic acid bacteria (*Lactobacillus rhamnosus, Lactobacillus delbrueckii spp. Bulgaricus, Bifidobacterium lactis*), *Saccharomyces cerevisiae* | LAB pool (30 min): 11.5 ±2.3% LAB (60 min): 11.7 ± 4.4%, Saccharomyces: (30 min), 90.3 ± 0.3%, Saccharomyces: 60 min, 92.7 ± 0.7% | $AFM_1$ | 0.5 ng $AFM_1$ $mL^{-1}$, LAB pool: $10^{10}$ cells $mL^{-1}$ Yeast: $10^9$ cells $mL^{-1}$ Contact time: 30 min or 60 min | Corassin *et al.*, 2013 |
| Fermented milk drink | *Lactobacillus casei Shirota* | $AFB_1$-lys reduction: 82.37% | Serum $AFB_1$-lysine adduct | 4-week intervention phases, (A): probiotic drinks 2 twice a day (B): placebo for 6, 8, or 10 weeks | Redzwan *et al.*, 2016 |
| Doogh | *Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus casei, , Bifidobacterium lactis* | Day 28, *Lactobacillus acidophilus*: 98.8 ± 1.3% | $AFM_1$ | 0.500 ppb toxin, 1,14, or 28 days at 5 °C, *L. acidophilus* 9 log cfu/mL | Sarlak *et al.*, 2017 |
| Ergo fermented milk | *L. plantarum Lactobacillus acidophilus, Lactobacillus brevis, Lactobacillus casei* subsp. *casei, Lactobacillus helveticus, Streptococcus faecalis, Streptococcus thermophiles, Leuconostoc mesenteroides,* subsp. *cremoris* | 57.33% 54.04% | $AFM_1$ | Time: 1–5 days Temperature: 25°C | Shigute and Washe, 2018 |

$AFM_1$: Aflatoxin $M_1$, $AFB_1$: Aflatoxin $B_1$, OA: Ochratoxin A, ZEA: Zearalenone, $AFG_1$: Aflatoxin $G_1$.

**Table 5. Heavy metals decontamination in milk and dairy products.**

| Product | Microorganism | Contaminant | Removal% W/W | Conditions | Reference |
|---|---|---|---|---|---|
| Milk | *Saccharomyces cerevisiae* | Pb | 70% | Opt. at $22\times10^8$ CFU inoculation of yeast, Lead content 70 µg/l | Massoud *et al.*, 2019 |
| Kefir | *Lactococcus lactis, Kluyveromyces marxianus,* co-culture | Ni, Cu, Cd, Pb, Fe | 81.53%, 73.45%, 79.48%, 68.53%, 58.17% | Time: 10 days | Cherni *et al.*, 2020 |
| Milk | *Saccharomyces cerevisiae* | Cd | 70% | Cadmium content in milk 80 µg/L, $30\times10^8$ CFU *Saccharomyces cerevisiae,* storage time the 4th day, | Masoud *et al.*, 2020 |
| Milk | *Lactobacillus acidophilus* | Pb Cd | 80% 75% | $1 \times 10^{12}$ CFU of *L. acidophilus*, in 4 days with the initial pollution of 100 µg/L. | Massoud *et al.*, 2020b |
| Milk | *Saccharomyces cerevisiae* | Hg | 70% | Contact time: 30 days, initial concentration of Hg: 80 µg/L and biomass dosage $22 \times 10^8$ CFU | Massoud *et al.*, 2021 |

Lead: Pb, Nickel: Ni, Copper: Cu, Cadmium: Cd, Iron: Fe, Mercury: Hg.

(Massoud *et al.*, 2020a). Therefore, they have introduced applying *S. cerevisiae* as a novel and useful technology for the bioremoval of heavy metals from foodstuff (Massoud *et al.*, 2019, 2020a)

Different treatments, such as caustic, ethanol, acidic, and heat, can enhance the biosorption of heavy metals by microorganisms. In a study by Yekta Göksungur *et al.* (2005), "potential of baker's yeast in bioremoval of cadmium and lead with 3 pretreatments (caustic, heat and ethanol)" was examined. Ethanol-treated yeast strains could remove the most content of metals and it can be explained by improving the availability of yeast binding sites and maybe enhancing the metals accessibility (Göksungur *et al.*, 2005).

## Mechanisms of Bioremoval and Stability of Complexes (Probiotics/Starters-heavy Metal/Toxin)

$AFM_1$ and other toxins are accumulated in milk and dairy products because they are able to bind to milk protein components such as casein (Dyomina *et al.*, 2017; Granados-Chinchilla, 2016; Sarlak *et al.*, 2017). Therefore, numerous investigations have been focused on the removal of toxins using microorganisms, such as LAB (Dyomina *et al.*, 2017; Sarlak *et al.*, 2017).

Although the mechanism of bioremoval of toxins and heavy metals by LAB was not well known until now, it is proposed that toxins are highly linked by cell wall components of microorganisms and are not metabolically degraded (Zoghi *et al.*, 2014). Yeast and LAB are used widely to reduce toxins and metal ions. As both viable and dead cells are capable of adsorbing toxins, it is sensible to conclude that the removal of toxins is by adhesion to the components of microorganism's cell wall relative to covalent binding, as reviewed by Shetty *et al.* (2006) (Shetty and Jespersen, 2006). It is indicated that mannan components of the *S. cerevisiae* cell wall play an important role in toxin binding (Devegowda *et al.*, 1996). Generally, the cell wall proteins of *S. cerevisiae* are bound to β-1,3-glucans by covalent linkage by β-1,6-glucan chains (Shetty and Jespersen, 2006). Apart from this, the major part of the LAB cell is made up of peptidoglycan, which contains teichoic and lipoteichoic acids. Also, a proteinous S-layer and neutral polysaccharides as components of the LAB cell wall have been recognized and reviewed by Lahtinen *et al.* (2004).

A study by Yiannikouris *et al.* (2004) indicated the interactions between zearalenone and β-D-glucans, in which β-1,3 D-glucan chains constitute a stable helical link with zearalenone and stabilized by β-1,6 D-glucan chains (Yiannikouris *et al.*, 2004). In order to investigate the mechanism of binding of aflatoxins to *L. rhamnosus* it is indicated that carbohydrates in the cell wall are predominantly responsible for binding to aflatoxins. In samples treated by urea, it is shown that hydrophobic interactions play a significant role in binding, and treatment by NaCl and $CaCl_2$ showed that electrostatic interactions played a minor role (Haskard *et al.*, 2000).

Also, it is stated that $AFM_1$ is bound to LAB cell wall components by weak noncovalent interactions. The difference in the binding ability among different microorganisms is attributed to the cell wall and cell envelope structures (El Khoury *et al.*, 2011). Similarly, Turbic *et al.* (2002) mentioned that the different binding ability of LAB highly depended on the strain of the microorganisms (Turbic *et al.*, 2002).

Another study associated with the mechanism of biosorption illustrated that nonviable cells, including heat and acid-treated cells, produced complexes with higher stability, which means better access of groups in treated cells rather than viable ones. This phenomenon emphasizes that the viability of cells is not an important factor for the binding ability of cells (Haskard *et al.*, 2001). Furthermore, it is shown that acids might be capable of breaking amine binding in peptides and proteins, which leads to the production of peptides and even amino acids, and consequently, more accessible aflatoxin binding sites will be available (El-Nezami *et al.*, 2002). Similarly, it is noted that hydrophobic interactions are highly expected in LAB, which is treated by acid because acid treatment leads to denaturation of proteins and enhanced hydrophobic binding sites (Haskard *et al.*, 2000).

Moreover, the mechanisms of bioremoval could be influenced by various factors including types of microorganisms or even the status of biomass (living or nonliving microorganism), chemical properties of toxic materials, and environmental factors, such as temperature as well as pH (Javanbakht *et al.*, 2014).

For more illustration, Javanbakht *et al.* (2014) investigated the mechanism of removal of heavy metals by microorganisms. They suggested that two different types of pathways are involved in biosorption, which depends on cell metabolism and is divided into metabolism-dependent and metabolism-independent groups. The first pathway only occurs in viable cells through the transformation of metals across the cell wall. The second mechanism is involved in the physicochemical interaction between metals and functional groups of cell surface such as physical adsorption and ion exchange without depending on the cell metabolisms (Javanbakht *et al.*, 2014).

To investigate the stability of complexes, Haskard *et al.* (2001) evaluated the stability of 12 complexes between

LAB and $AFB_1$ considering both viable and nonviable cells and concluded that 71% of $AFB_1$ remained bound, indicating the high stability of the complexes. Also, they showed that nonviable cells retained a higher amount of $AFB_1$, as mentioned above (Haskard *et al.*, 2001). Based on their results, the stability of complexes depends upon three factors including strain, treatment type, and environmental conditions. Fazeli *et al.* (2009) conducted a study to investigate the effect of strains, including *L. casei*, *L. plantarum*, and *L. fermentum*, on the reduction of $AFB_1$ and concluded that all the strains were able to remove $AFB_1$, although *L. casei* was found to be a stronger binder of $AFB_1$ rather than other bacteria (Fazeli *et al.*, 2009).

A Study by Zoghi *et al.* (2020) showed that adsorption of patulin by LAB can be reversible in simulated gastrointestinal conditions. The reversibility of binding between LAB and patulin can be explained by the sense of noncovalent electrostatic bonds (Van der Waals and hydrogen bonds) (Zoghi *et al.*, 2020). Similarly, in another study, the adsorption of $AFB_1$, zearalenone, and ochratoxin A by kefir grains in simulated gastrointestinal pH was reversible. In pH 3, further amounts of toxins were released (Taheur *et al.*, 2017). Moreover, reduction of $AFB_1$ from a gastrointestinal model by several cells, including *L. rhamnosus, L. plantarum,* and *L. acidophilus*, were examined by Motameny *et al.* (2012), and they concluded that *L. plantarum* was the most active cell (Motameny *et al.*, 2012).

## Conclusions

Aflatoxins and heavy metals frequently contaminate milk and dairy products at different levels. In the food industry, controlling aflatoxin and heavy metal levels in dairy products is a challenge for researchers. According to the recent studies summarized in this review, it is revealed that using different microorganisms (such as probiotics) in different dairy products could result in the removal of toxins and heavy metals by creating bonds between contaminants and these microorganisms. Using the starters in fermented dairy products can be helpful in the decontamination of toxins and heavy metals. According to this review, *L. bulgaricus*, Kefir grains, *L. acidophilus*, and *L. rhamnosus* could be useful for decreasing $AFM_1$ and other toxins in milk and dairy products. Also, for decontamination of heavy metals, kefir grains had the best ability for the bioremoval of different metals.

## Future directions

More investigations are needed regarding the stability of binding between probiotics and toxins/heavy metals in *in vivo* and *in vitro* conditions. Also, more experiments should be done for finding optimum conditions for special starters in special dairy products for better decontamination.

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### Availability of data and material

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### Code availability

Not applicable.

## Authors' Contributions

RM was involved in writing and original draft preparation; AZ was responsible for writing, review, and editing; KKD was concerned with conceptualization and supervision; FM was involved in writing and editing; and SJ, RM, and YR were responsible for review and editing.

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