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## Novel strategies for degradation of aflatoxins in food and feed: A review

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### ABSTRACT

Aflatoxins are toxic secondary metabolites mainly produced by *Aspergillus* fungi, posing high carcinogenic potency in humans and animals. Dietary exposure to aflatoxins is a global problem in both developed and developing countries especially where there is poor regulation of their levels in food and feed. Thus, academics have been striving over the decades to develop effective strategies for degrading aflatoxins in food and feed. These strategies are technologically diverse and based on physical, chemical, or biological principles. This review summarizes the recent progress on novel aflatoxin degradation strategies including irradiation, cold plasma, ozone, electrolyzed oxidizing water, organic acids, natural plant extracts, microorganisms and enzymes. A clear understanding of the detoxification efficiency, mechanism of action, degradation products, application potential and current limitations of these methods is presented. In addition, the development and future perspective of nanozymes in aflatoxins degradation are introduced.

### 1. Introduction

Aflatoxins (AFs) are a class of carcinogenic mycotoxins produced by the *Aspergillus* species, notably *Aspergillus flavus* and *A. parasiticus*, and are commonly found in staple food crops such as corn, rice, peanuts, dried fruits and spices as well as milk products (Ismail et al., 2018; Reddy et al., 2010; Rushing & Selim, 2019). They were first discovered in the early 1960s as the principal etiological agents of "Turkey X disease" resulting in the deaths of over 100,000 turkeys in England (Blount, 1961). Both *A. flavus* and *A. parasiticus* produce aflatoxin B<sub>1</sub> (AFB<sub>1</sub>) and aflatoxin B<sub>2</sub> (AFB<sub>2</sub>); *A. parasiticus* also produces aflatoxin G<sub>1</sub> (AFG<sub>1</sub>) and aflatoxin G<sub>2</sub> (AFG<sub>2</sub>). Among the four toxins, AFB<sub>1</sub> is the most harmful and is responsible for more than 75% of all aflatoxins related food and feed contamination (My & Sachan, 1997). In the liver, AFB<sub>1</sub> undergoes cytochrome P450-mediated metabolism, including the epoxidation to AFB<sub>1</sub>-exo-8, 9-epoxide and AFB<sub>1</sub>-endo-8, 9-epoxide, hydroxylation to aflatoxin M<sub>1</sub> (AFM<sub>1</sub>) and aflatoxin Q<sub>1</sub> (AFQ<sub>1</sub>), and demethylation to aflatoxin P<sub>1</sub> (AFP<sub>1</sub>) (Bbosa, Kitya, Odda & Ogwai-Okeng, 2013). AFB<sub>1</sub>-exo-8, 9-epoxide covalently binds to DNA, proteins and phospholipids to form adducts, resulting in genetic, metabolic, signaling and cell structure disruptions (Benkerroum, 2020). The wide range of toxic effects caused by aflatoxin exposure is named aflatoxicosis and has been described in two forms: (i) "acute intoxication" caused by short exposure to high amount of aflatoxins and characterized by serious liver damage, jaundice, haemorrhage, oedema and eventually death; (ii) "chronic

sublethal exposure," which leads to immunosuppression, nutritional disorders and cancer (Marchese et al., 2018).

The International Agency for Research on Cancer (IARC) has classified AFB<sub>1</sub> as a Group I human carcinogen (Ostry, Malir, Toman, & Grosse, 2017). Globally more than 5 billion people are chronically exposed to AFB<sub>1</sub> (Pandey et al., 2019). The annual global burden of AFB<sub>1</sub>-induced human hepatocellular carcinoma (HCC) is as high as 155,000 cases, with most occurring in Sub-Saharan Africa and Southeast Asia (Liu & Wu, 2010). In China, liver cancer is the second most prevalent cancer, accounting for 19.33% of all kinds of cancers (Chen & Zhang, 2011). Prospective cohort studies have revealed that the major causative factors associated with primary liver cancer in endemic area of China are chronic infection with hepatitis B virus (HBV) and extended exposure to high levels of aflatoxins in the diet (Chen et al., 2013). While AFB<sub>1</sub> is likely to be only a minor risk factor for HCC development in Europe, chronic exposure to AFB<sub>1</sub> may nevertheless impair immune system and child growth (EFSA, 2007). Considering the potential damage of dietary aflatoxins to the consumer health, many countries and regions have imposed maximum limits for aflatoxins in food and feed. The U.S. Food and Drug Administration (FDA) has specified the maximum acceptable limit of 20 µg kg<sup>-1</sup> for total AFs in all food except milk (FDA, 2011). In the European Community (EC), even more stringent regulations have been established, with the maximum permissible levels of 2 and 4 µg kg<sup>-1</sup> for AFB<sub>1</sub> and total AFs, respectively, in peanuts, dried fruits and cereals for direct human consumption or as ingredients

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in food (EC, 2010). In China, the legal limits for AFB<sub>1</sub> in cereal products intended for human consumption range from 5 to 10 µg kg<sup>-1</sup> whereas levels in animal feedstuffs are allowed to be much higher, reaching upwards from 20 to 50 µg kg<sup>-1</sup> (Ma et al., 2018).

Current strategies to reduce the risk of consumer exposure to aflatoxins can be divided into pre-harvest prevention of aflatoxins production and post-harvest aflatoxins elimination. The application of Good Manufacturing Practices (GAPs), i.e., the use of fertilizers, pest control and fungal-resistant crop varieties, harvesting at the right time and maintaining low moisture content and temperature during storage can inhibit mold growth and aflatoxins production in grains. However, these prevention strategies are not always effective to achieve aflatoxin-free food and feed. This emphasizes the need of post-harvest intervention to eliminate aflatoxin contamination. Conventional food processing methods like sorting, cleaning, dehulling and milling can only remove highly contaminated fractions from bulk materials (Karlovsky et al., 2016). The decomposition temperatures of aflatoxins range from 237 to 306 °C (Rustom, 1997). Thus, aflatoxins are quite resistant to ordinary cooking, frying, baking and roasting (Kabak, 2009). The use of aflatoxin binders for the prevention of aflatoxicosis has become popular in animal nutrition. Several reports documented that mineral adsorbents like bentonite, zeolite, montmorillonite and aluminosilicate could partly or fully counteract the toxic effects of dietary aflatoxins in farm animals (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011; Vekiru et al., 2015). However, these mineral adsorbents may also bind vitamins, minerals and amino acids. Furthermore they may induce cytotoxic effects such as oxidative stress, reduction in cell viability, apoptosis, and DNA damage (Elliott, Connolly, & Kolawole, 2019). Organic adsorbents based on yeast and bacterial cell wall have also been used to bind aflatoxins but further studies are needed to improve their binding specificity for aflatoxins (Luo, Liu, Yuan, & Li, 2020). As aflatoxicosis continues to be a problem in humans and animals, several novel strategies have been developed and optimized over the past decade that show promise in degrading aflatoxins in food and feed. These strategies can be broadly categorized as physical, chemical and biological (Umeshah et al., 2017; Udomkun et al., 2017). Physical approaches based on advanced oxidation technology such as irradiation and cold plasma allow for rapid degradation of aflatoxins (Calado, Venâncio, & Abrunhosa, 2014; Gavahian & Cullen, 2019). Chemical means involve the use of ozone, electrolyzed oxidizing water, organic acids and natural plant extracts, which are widely accepted as safe food additives in many countries like China and the USA (Diao, Hou, & Dong, 2013; Rahman, Khan, & Oh, 2016; Lee, Her, & Lee, 2015; Loi, Paciolla, Logrieco, & Mulè, 2020). Biological methods take the form of microbial and enzymatic transformation of aflatoxins into non-toxic or less toxic metabolites (Ji, Fan, & Zhao, 2016; Kumar, Mahato, Kamle, Mohanta, & Kang, 2016). In this paper, our aim is to provide an updated and comprehensive review of these novel aflatoxin degradation technologies. Moreover, we will provide a brief description about recent development of nanozymes in aflatoxins degradation.

## 2. Physical degradation of aflatoxins

### 2.1. Degradation of aflatoxins by irradiation

In general irradiation can be classified into two forms: ionizing (e.g. X-rays, ultraviolet rays, gamma rays, and electron beam) and non-ionizing irradiation (e.g. radio waves, microwaves, infrared waves, and visible light waves). Extensive research has been performed to apply irradiation technology for eliminating mycotoxins. Table 1 presents the outcomes from recent studies on aflatoxin degradation in food and feed by irradiation.

#### 2.1.1. Degradation of aflatoxins by gamma irradiation

Gamma rays are electromagnetic radiation emitted from the decay of an unstable source such as a radioactive isotope (e.g., <sup>60</sup>Co, <sup>192</sup>Ir, <sup>137</sup>Cs,

**Table 1**

Summary of recent studies (2010 to date) on aflatoxins degradation in food and feed with irradiation.

Treated sample	Treatment parameters	Aflatoxin (µg kg <sup>-1</sup> or µg L <sup>-1</sup> )	Degradation (%)	Reference
<b><sup>60</sup>Co gamma</b>				
Corn	10 kGy	AFB <sub>1</sub> (57–1210)	85.6–98.6	(Markov et al., 2015)
Corn	8 kGy	AFB <sub>1</sub> (50.4)	60.3	(Mohamed, El-Dine, Kotb, & Saber, 2015)
Wheat	8 kGy	AFB <sub>1</sub> (37.6)	69.3	
Rice	8 kGy	AFB <sub>1</sub> (27.5)	64.7	
Peanut	9 kGy	AFB <sub>1</sub> (300)	43	(Patil, Shah, Hajare, Gautam, & Kumar, 2019)
Brazil nut	10 kGy	AFB <sub>1</sub> (4.8)	84.2	(Assuncao, Reis, Baquiao, & Correa, 2015)
Red chilli	6 kGy	AFB <sub>1</sub> (11–35)	86–98	(Iqbal et al., 2013)
Dried hot pepper	6 kGy	AFT (1.1)	6	(Iqbal, Amjad, Asi, & Arino, 2012)
White pepper	30 kGy	AFB <sub>1</sub> (60), AFB <sub>2</sub> (18), AFG <sub>1</sub> (60) and AFG <sub>2</sub> (18)	50.6, 35.2, 47.7 and 42.9	(Janili, Jinap, & Noranizan, 2012)
Black pepper	30 kGy	AFB <sub>1</sub> (60), AFB <sub>2</sub> (18), AFG <sub>1</sub> (60) and AFG <sub>2</sub> (18)	47.2, 39.4, 47.4 and 40.4	
Almond	15 kGy	AFB <sub>1</sub> (20), AFB <sub>2</sub> (25), AFG <sub>1</sub> (20) and AFG <sub>2</sub> (20)	19.3, 11.0, 21.1 and 16.6	(Vita, Rosa, & Giuseppe, 2014)
Cattle feed	10 kGy	AFB <sub>1</sub> (50)	85	(Markov et al., 2015)
Poultry feed	15 kGy	AFB <sub>1</sub> (25), AFB <sub>2</sub> (25), AFG <sub>1</sub> (25) and AFG <sub>2</sub> (25)	18.2, 11.0, 21.1 and 13.6	(Di Stefano, Pitonzo, Cicero, & D'Oca, 2014)
<b>Electron beam</b>				
Peanut	300 kGy	AFB <sub>1</sub> (1000)	70	(Liu et al., 2018)
Brazil nut	10 kGy	AFB <sub>1</sub> (4.8)	65.7	(Assuncao, Reis, Baquiao, & Correa, 2015)
<b>Ultraviolet</b>				
Wheat	254 nm at 0.1mW cm <sup>-2</sup> for 160 min	AFT (13–23)	65–90	(Ghanghro, Nizamani, Channa, Ghanghro, & Sheikh, 2016)
Red chilli powder	365 nm for 60 min	AFB <sub>1</sub> (1872)	87.8	(Tripathi & Mishra, 2010)
Peanut	254 nm for 10 h	AFB <sub>1</sub> (350)	99.1	(Garg, Aggarwal, Javed, &

(continued on next page)

Table 1 (continued)

Treated sample	Treatment parameters	Aflatoxin ( $\mu\text{g kg}^{-1}$ or $\mu\text{g L}^{-1}$ )	Degradation (%)	Reference
Peanut	220–400 nm at 0.8 mW $\text{cm}^{-2}$ for 80 min	AFB <sub>1</sub> (2000)	100	(Khandal, 2013) (Chang, Jin, Liu, Liu, & Wang, 2013)
Peanut oil	220–400 nm at 0.8 mW $\text{cm}^{-2}$ for 30 min	AFB <sub>1</sub> (2000)	100	(Liu et al., 2011)
Peanut oil	365 nm at 6.4 mW $\text{cm}^{-2}$ for 10 min	AFB <sub>1</sub> (52.0)	86.1	(Diao et al., 2015b)
Peanut oil	365 nm at 55–60 mW $\text{cm}^{-2}$ for 20 min	AFB <sub>1</sub> (128)	96	(Mao et al., 2016)
Peanut oil	254 nm for 120 min	AFB <sub>1</sub> (83)	35.1	(Xu, Ye, Cui, Song, & Xie, 2019)
<b>Photocatalysis</b>				
Peanut oil	TiO <sub>2</sub> layer in a closed-loop reactor; 254 nm for 120 min	AFB <sub>1</sub> (83)	60.4	(Xu, Ye, Cui, Song, & Xie, 2019)
Peanut oil	Immobilized TiO <sub>2</sub> ; UV of 92 mW $\text{cm}^{-2}$ and visible of 200 mW $\text{cm}^{-2}$ for 4 min	AFB <sub>1</sub> (674.3) and AFB <sub>2</sub> (311.6)	100	(Magzoub et al., 2019)
<b>Pulsed light</b>				
Rough rice	0.52 J $\text{cm}^{-1}$ per pulse for 80 s	AFB <sub>1</sub> (132) and AFB <sub>2</sub> (45)	75.0 and 39.2	(Wang et al., 2016)
Rice bran	0.52 J $\text{cm}^{-1}$ per pulse for 15 s	AFB <sub>1</sub> (36) and AFB <sub>2</sub> (4.4)	90.3 and 86.7	
Peanut oil	0.4 J $\text{cm}^{-1}$ per pulse for 800 s	AFT (40)	78	(Abuagela, Iqdam, Baker, & MacIntosh, 2018)
<b>Microwave</b>				
Alkalized corn	1650 W for 5.5 min	AFB <sub>1</sub> (22.5) and AFB <sub>2</sub> (69.6)	36 and 58	(Pérez-Flores, Moreno-Martínez, & Méndez-Albores, 2011)
Corn flour	Heating in microwave oven for 10 min	AFB <sub>1</sub> (100)	67.7	(Alkadi & Altal, 2019)
Peanut	480 W for 5 min	AFB <sub>1</sub> (300)	67	(Patil, Shah, Hajare, Gautam, & Kumar, 2019)
Peanut	Heating in microwave oven at 92 °C for 5 min	AFB <sub>1</sub> (5–183) and AFB <sub>2</sub> (7–46.7)	50–60 and 100	(Mobeen, Aftab, Asif, & Zuzzer, 2011)

AFB<sub>1</sub>, Aflatoxin B<sub>1</sub>; AFB<sub>2</sub>, Aflatoxin B<sub>2</sub>; AFG<sub>1</sub>, Aflatoxin G<sub>1</sub>; AFG<sub>2</sub>, Aflatoxin G<sub>2</sub>; AFT, Total aflatoxins, the sum of AFB<sub>1</sub>, AFB<sub>2</sub>, AFG<sub>1</sub> and AFG<sub>2</sub>.

and <sup>70</sup>Tm). Gamma rays are the preferred source of irradiation for food processing because of their high reactivity and penetrability. The irradiation of food up to an overall dose of 10 kGy causes no toxicological hazards and no special microbiological or nutritional problems (WHO, 1999). Gamma irradiation can facilitate radiolysis of water and generation of highly reactive free radicals like radical hydrogen (H<sup>•</sup>), superoxide radical (O<sub>2</sub><sup>•-</sup>) and hydroxyl ion (OH<sup>-</sup>), which play an important role in the destruction of aflatoxins (Rustom, 1997). A study conducted by Wang et al. (2011) examined the structure of AFB<sub>1</sub> radiolytic products. This analysis revealed that the double bond of the terminal furan ring was no longer in existence in most of radiolytic products due to free-radical addition reaction during gamma irradiation. The double bond in the terminal furan ring of AFB<sub>1</sub> is known to be associated with its toxicity. In the liver, the oxidation of the double bond in the terminal furan ring of AFB<sub>1</sub> by hepatic cytochrome P450 enzymes (CYPs) yields AFB<sub>1</sub>-exo-8, 9-epoxide, which can react with the N<sup>7</sup> atom of guanine to generate pro-mutagenic DNA adducts (Bbosa, Kitya, Odda & Ogwali-Okeng, 2013). Thus, the loss of the double bond of the terminal furan ring in AFB<sub>1</sub> after gamma irradiation treatment led to a significant reduction of its cytotoxicity in Pk15, HepG2 and SH-SY5Y cells (Domijan et al., 2019).

The efficiency of gamma irradiation-assisted degradation of aflatoxins depends on many factors, such as radiation dose, mycotoxin concentration, water content and matrix composition. Most of the studies in the literature concluded that gamma irradiation at levels ranging from 5 to 10 kGy could eliminate a significant amount of aflatoxins in food products (Table 1). Iqbal et al. (2013) studied the efficiency of aflatoxins degradation in red chillies through gamma irradiation and observed that the application of 6 kGy reduced the level of AFB<sub>1</sub> by more than 86%. Similarly, Markov et al. (2015) reported that the treatment of corn with gamma ray at 5 kGy resulted in a 69.8% reduction of AFB<sub>1</sub> level, while the dose of 10 kGy detoxified AFB<sub>1</sub> by 94.5%. The experiments performed by Assuncao, Reis, Baquiao, and Correa (2015) also showed that gamma irradiation at 5 to 10 kGy was sufficient to eliminate 70.6 to 84.2% of AFB<sub>1</sub> in Brazil nuts. Other studies nevertheless showed that gamma irradiation is not very effective in aflatoxins degradation. Jalili, Jinap, and Noranizan (2012) reported that gamma irradiation at a dose of 10 kGy did not significantly affect the aflatoxins content in black and white pepper. In addition, Di Stefano, Pitonzo, Cicero, and D'Oca (2014) conducted gamma irradiation study with poultry feed and obtained only 18.2, 11.0, 21.1 and 13.6% reduction of AFB<sub>1</sub>, AFB<sub>2</sub>, AFG<sub>1</sub> and AFG<sub>2</sub>, respectively, with a dose of 15 kGy. Gamma irradiation also presents high microbial inactivation capacity, thus allowing the reduction of microbial load and extension of food shelf life. The interest in the adoption of gamma irradiation in food decontamination is increasing as consumers are beginning to appreciate the benefits of irradiated food. Up to now, more than 55 countries including China, USA, Japan and European countries have approved this technology in food processing under certain conditions (Priyadarshini, Rajauria, O'Donnell, & Tiwari, 2019). However, gamma irradiation seems to be not suitable for food with high lipid and vitamin content, mainly due to the extensive peroxidation of unsaturated bonds in the polyunsaturated fatty acids, resulting in the increase of the onset of oxidative rancidity in food (Caulfield, Cassidy, & Kelly, 2008).

### 2.1.2. Degradation of aflatoxins by electron beam irradiation

Electron beam (EB) irradiation has also shown potential for degrading aflatoxins, and this technology has the advantages of short processing time, low equipment costs, and dosage control. EB irradiation of AFB<sub>1</sub> in an acetonitrile solution resulted in the formation of two degradation products, C<sub>14</sub>H<sub>12</sub>O<sub>5</sub> and C<sub>17</sub>H<sub>14</sub>O<sub>5</sub> (Wang et al., 2015a). In an aqueous solution, the reduction of AFB<sub>1</sub> by EB irradiation led to the generation of five by-products, with a loss of the double bond in the terminal furan ring in four of the five products (Liu et al., 2016). Preliminary safety assessments of the degradation products conducted with the Ames test and 3-(4,5-Dimethylthiazol-2-yl)-2,5-

diphenyltetrazolium bromide (MTT) viability assay, showed that the mutagenicity and cytotoxicity of EB-irradiated AFB<sub>1</sub> were significantly decreased. Nevertheless, the decontamination efficiency of EB irradiation is less than that of gamma irradiation. Gamma irradiation at doses of 5 and 10 kGy reduced AFB<sub>1</sub> content in Brazil nuts by 70.6 and 84.2%, respectively, whereas EB irradiation at the same doses resulted in AFB<sub>1</sub> reduction by 53.3 and 65.7%, respectively (Assuncao, Reis, Baquiao, & Correa, 2015). Additionally, Liu et al. (2018) found that EB irradiation was not very effective in degrading AFB<sub>1</sub> in peanut meal, since an irradiation dose of 300 kGy, which was ten times of the maximum allowable dosage permitted by FDA, was required for achieving a 70% reduction of AFB<sub>1</sub>.

### 2.1.3. Degradation of aflatoxins by ultraviolet irradiation

Ultraviolet (UV) irradiation has been known for decades as an effective physical method for the destruction of aflatoxins due to their photosensitivity. As a non-thermal food decontamination technology, UV irradiation offers the advantages of being practical and cost effective, and eco-friendly as it exhibits no toxic effects and no waste generation (Gayán, Condón, & Álvarez, 2014). AFB<sub>1</sub> absorbs UV rays at 222, 265 and 362 nm, with the absorption maxima at 362 nm (Samarajeewa, Sen, Cohen, & Wei, 1990). The formation of hydroxyl free radicals (OH<sup>•</sup>) initiated by UV irradiation could attack the terminal double bond at the C8-C9 position of AFB<sub>1</sub> (Liu et al., 2010), and the photodegradation pathway of AFB<sub>1</sub> in water under UV irradiation was depicted in Fig. 1. The results of the Ames test and cell viability assay indicated that the mutagenicity and cytotoxicity of the photodegradation products were much lower than that of AFB<sub>1</sub> (Diao et al., 2015b; Mao et al., 2016). UV intensity and irradiation duration are key factors affecting aflatoxins elimination efficiency. UV irradiation at 800 μw cm<sup>-2</sup> for 30 min was sufficient to completely remove AFB<sub>1</sub> in peanut oil, whereas the toxin

was reduced by about 79 and 85% at the intensity of 200 and 400 μw cm<sup>-2</sup>, respectively (Liu et al., 2011). The treatment of peanuts with UV light at 254 nm was found to reduce AFB<sub>1</sub> level by 59.7% within 2 h, and by up to 99.1% after 10 h (Garg, Aggarwal, Javed, & Khandal, 2013). Moreover, Ghanghro, Nizamani, Channa, Ghanghro, and Sheikh (2016) showed that more than 80% of aflatoxins in wheat samples were eliminated when exposed to UV short wave at 254 nm for 160 min. In general, the application of moderate doses of UV irradiation does not cause extensive adverse effects on the physicochemical and sensory characteristics of food products (Delorme et al., 2020). UV light can easily penetrate through clear or transparent liquids. Nevertheless, its penetration capacity into solid materials is limited, which results in low decontamination efficiency in food products with high content of suspended solids (Fan, Huang, & Chen, 2017). Thus, opaque or granular food products need to be presented as a thin layer during UV irradiation detoxification (Diao et al., 2015a).

### 2.1.4. Degradation of aflatoxins by photocatalysis

Several recent studies have demonstrated that the use of UV-visible irradiation in combination with semiconducting photocatalysts can increase the efficiency of aflatoxins degradation in liquid matrix (Sun, Zhao, Xie, & Liu, 2019; Xu, Ye, Cui, Song, & Xie, 2019). During the photocatalytic degradation process, the photo-generated valence band holes (h<sup>+</sup>), hydroxyl free radicals (OH<sup>•</sup>) and superoxide radical (O<sub>2</sub><sup>•-</sup>) are capable of directly oxidizing AFB<sub>1</sub> (Sun, Zhao, Xie, & Liu, 2019; Mao et al., 2018). The most widely used photocatalyst is TiO<sub>2</sub>, as it is highly active under UV irradiation, non-toxic, highly efficient, and has long-term photostability. Sun, Zhao, Xie, and Liu (2019) evaluated photocatalytic degradation of AFB<sub>1</sub> in methanol by activated carbon supported TiO<sub>2</sub> catalyst (AC/TiO<sub>2</sub>) under UV-Vis light. The degradation rate reached 95% within 120 min by UV-Vis irradiation in the presence

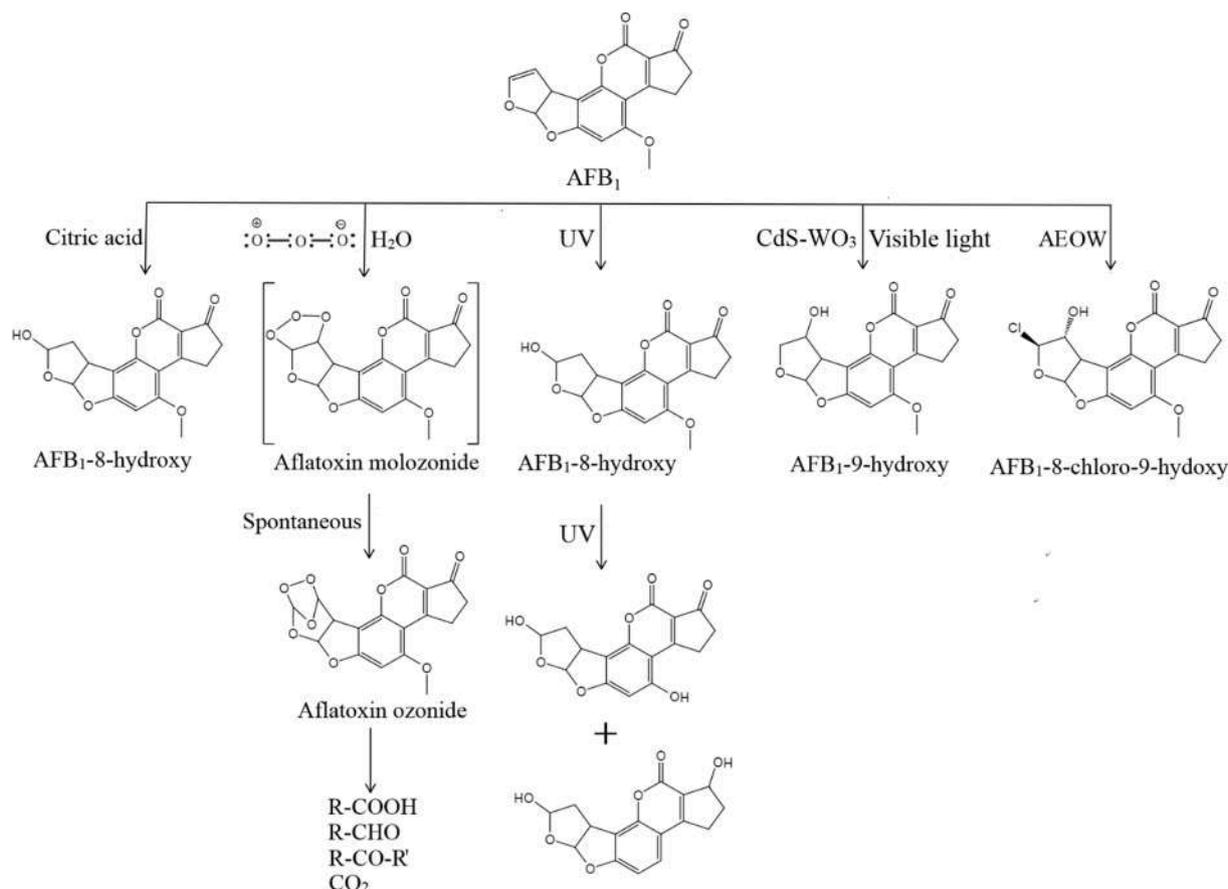


Fig. 1. The degradation pathways of AFB<sub>1</sub> by several physical and chemical treatments.

of AC/TiO<sub>2</sub> (6 mg mL<sup>-1</sup>), whereas only 50% of AFB<sub>1</sub> was degraded by UV-Vis irradiation alone. Xu et al. (2019) designed an immobilized-bed photocatalytic reactor consisting of a glass tube coated with TiO<sub>2</sub> for the detoxification of AFB<sub>1</sub> in contaminated peanut oil. Approximately 60.4% removal of AFB<sub>1</sub> was achieved within 120 min by employing this TiO<sub>2</sub>/UV system, which was higher than that of UV photolysis alone (35.1%). In a study of Magzoub et al. (2019), AFB<sub>1</sub> and AFB<sub>2</sub> in Sudanese peanut oil were almost completely removed by immobilized TiO<sub>2</sub> within 4 min using UV-Vis light. Additionally, the physicochemical characteristics of peanut oil, including fatty acids composition, free fatty acids content, peroxide value, saponification value, acid value, iodine value, moisture and volatile matters as well as the refractive index did not significantly change during the photocatalytic treatment.

The major disadvantage of TiO<sub>2</sub> photocatalyst is its restriction to UV irradiation, which accounts for only 4% of the sunlight spectrum. Thus, efforts have been devoted to developing visible-light-driven photocatalysts for aflatoxins reduction. Jamil, Abbas, Nasr, El-Kady, and Ibrahim (2017) successfully synthesized Sc-doped SrTi<sub>0.7</sub>Fe<sub>0.3</sub>O<sub>3</sub> nanoparticles and studied their performance as a photocatalyst in the degradation of AFB<sub>1</sub>. The results showed that AFB<sub>1</sub> could be completely degraded into carbon dioxide and water by 10 mol% Sc-doped SrTi<sub>0.7</sub>Fe<sub>0.3</sub>O<sub>3</sub> under visible light with a detoxification rate of 88.2% within 120 min. Mao et al. (2018) reported that nanosized graphitic carbon nitride (g-C<sub>3</sub>N<sub>4</sub>) sheets exhibited a significantly enhanced photocatalytic activity for the degradation of AFB<sub>1</sub> compared with bulk g-C<sub>3</sub>N<sub>4</sub> under visible light irradiation. This is due to better photogenerated charge separation and a larger surface area of nanosized g-C<sub>3</sub>N<sub>4</sub> sheets. After treatment for 120 min, the AFB<sub>1</sub> removal efficiency using nanosized g-C<sub>3</sub>N<sub>4</sub> sheets reached 70.2%, while it was only 30.8% for bulk g-C<sub>3</sub>N<sub>4</sub>. In another study of Mao et al. (2019), Clew-like WO<sub>3</sub> decorated with CdS nanoparticles showed superior activity for attacking the C9 site of the double bond in the terminal furan ring of AFB<sub>1</sub> under visible light irradiation, resulting in the formation of AFB<sub>1</sub>-9-hydroxy as the major photodegradation product (Fig. 1). Indeed, photocatalysis is a promising technology in AFB<sub>1</sub> degradation, but very little information exists on the stability and safety of photocatalysts.

### 2.1.5. Degradation of aflatoxins by pulsed light

Another non-thermal technology called pulsed light (PL) has also been employed for the decontamination of aflatoxins in food and feed. Pulsed light is an FDA-approved technology for the rapid and efficient surface decontamination of food products with an upper limit fluence of 12 J cm<sup>-2</sup> (FDA, 1996). This novel technology creates short, high-intensity flashes of broadband emission light (100–1100 nm) including ultraviolet, visible and infrared rays (Oms-Oliu, Martín-Beloso, & Soliva-Fortuny, 2010). The intensity of the emitted light is about 20, 000 times more intense than direct sunlight at sea-level (Dunn, Ott, & Clark, 1995). Moreau et al. (2013) reported that eight flashes of PL (light flux of 1 J cm<sup>-2</sup> during one 300 ms flash) degraded 92.7% of AFB<sub>1</sub> in water. Wang et al. (2016) treated rough rice and rice bran with PL at 0.52 J cm<sup>-1</sup> per pulse. PL treatment of rough rice for 80 s reduced AFB<sub>1</sub> and AFB<sub>2</sub> by 75.0 and 39.2% respectively, while a treatment time of 15 s reduced AFB<sub>1</sub> and AFB<sub>2</sub> in rice bran by 90.3 and 86.7% respectively. Using a brine shrimp lethality assay and the Ames fluctuation assay, Wang et al. (2016) further demonstrated that PL treatment inactivated the cytotoxicity and mutagenicity of AFB<sub>1</sub> and AFB<sub>2</sub>. Similarly, Abua-gela et al. (2018) observed a 91% reduction in aflatoxins in dehulled peanuts after PL treatment (0.4 J cm<sup>-1</sup> per pulse). Additionally, it was shown that PL treatment did not significantly affect the chemical qualities such as peroxide value, fatty acid content and acidity value of oil extracted from peanuts, although slight changes in peanut kernel color were noted. However, despite the progress mentioned above, the breakdown products of aflatoxins after PL treatment are still under investigation. Characterization of the possible photodegradation pathways of aflatoxins under PL treatment will provide deep insight into the degradation mechanism and kinetics of this technology. There is also a

need for designing cost-effective PL equipment capable of generating high UV output in order to apply this emerging technology at an industrial scale.

### 2.1.6. Degradation of aflatoxins by microwave heating

Microwaves are electromagnetic waves in frequencies ranging from 300 MHz to 300 GHz with wavelengths from 1 m to 1 mm. The frequency of a domestic microwave is 2450 MHz, while industrial microwave systems generally use either 915 or 2450 MHz. Microwave heating is a unique volumetric heating method, which transforms electromagnetic field energy into thermal energy through the polarization effect of the electromagnetic radiation (Soni, Smith, Thompson, & Brightwell, 2020). Microwaving has been widely applied in the drying, heating, cooking and extraction of food. Some reports also documented the use of microwave heating in degrading aflatoxins in food materials. Pérez-Flores, Moreno-Martínez, and Méndez-Albores (2011) evaluated the effect of microwave treatment during alkaline-cooking of aflatoxin-contaminated corn. The results showed that AFB<sub>1</sub> and AFB<sub>2</sub> were reduced by 36 and 58%, respectively, when the contaminated corn was microwave-heated at a power output of 1650 W for 5.5 min. Moreover, microwave cooking of peanut and peanut products, respectively, resulted in a 50 to 60% reduction of the level of AFB<sub>1</sub>, while AFB<sub>2</sub> content decreased to non-detectable limits (Mobeen, Aftab, Asif, & Zuzzer, 2011). Alkadi and Altal (2019) also recently documented the degradation of AFB<sub>1</sub> up to 67.7% in corn flour heated in a microwave oven for 10 min. Overall, microwave heating demonstrated moderate success in reducing aflatoxins levels in food commodities. Microwave manufacturers are able to customize equipment to specific applications and food product types. However, it has always remained a challenge to address the non-uniform temperature distribution during microwave heating, which may lead to the formation of cold and hot spots in the treated food (Menon, Stojceska, & Tassou, 2020). Aflatoxins in cold spots can not be effectively detoxified, while overheating in hot spots may cause nutritional losses and quality deterioration. More studies are also required to optimize the process parameters to increase the degradation efficiency along with structure elucidation and safety evaluation of the degradation products.

### 2.2. Degradation of aflatoxins by cold plasma

Plasma is a highly energized ionized gas, generally known as the fourth state of matter, consisting of electrons, ions, UV irradiation and reactive neutral species such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) (Kogelschatz, 2004). In general, plasma can be loosely categorized according to its temperature into thermal and cold (also referred to as non-thermal) plasma. The generation of cold plasma can be achieved by means of electrical discharges in gases at atmospheric pressure and a temperature range from 30 to 60 °C (Hertwig, Meneses, & Mathys, 2018). Moreover, cold plasma can be described by the system used to generate it, for example, corona discharge (CD), dielectric barrier discharge (DBD), atmospheric pressure plasma jets (APPJ), and radio frequency plasma (RFP) (Fridman, Chirokov, & Gut-sol, 2005).

This rather new technology has been shown to enable the rapid detoxification of aflatoxins at ambient temperature and pressure conditions (Gavahian & Cullen, 2019; Misra, Yadav, Roopesh, & Jo, 2019). Siciliano et al. (2016) used DBD N<sub>2</sub>-plasma to degrade aflatoxins inoculated on dehulled hazelnuts. The results showed that approximately 70% of AFB<sub>1</sub> and total aflatoxins were detoxified following 12 min exposure to a 1150 W plasma treatment. Moreover, the authors demonstrated that AFB<sub>1</sub> and AFG<sub>1</sub> were more sensitive to N<sub>2</sub>-plasma treatment compared to AFB<sub>2</sub> and AFG<sub>2</sub>, respectively. Another study using N<sub>2</sub>-plasma found that the performance of plasma in degrading AFB<sub>1</sub> was connected to processing time and plasma frequency (Sakudo, Toyokawa, Misawa, & Imanishi, 2017). According to the results, 15 min of N<sub>2</sub>-plasma treatment at 1.5 kpps reduced AFB<sub>1</sub> by more than 90% and

abolished its toxicity to HepG2 cells. Shi, Ileleji, Stroschine, Keener, and Jensen (2017) investigated the effects of carrier gas type (air and modified atmosphere gas containing 65% O<sub>2</sub>, 30% CO<sub>2</sub>, and 5% N<sub>2</sub>) and relative humidity (RH of 5, 40 and 80%) on AFB<sub>1</sub> degradation induced by high voltage atmospheric cold plasma (HVACP). The best result was observed while operating the plasma in a 40% RH modified atmosphere gas wherein 88.3% of AFB<sub>1</sub> in corn was eliminated within 5 min. In the case of peanut samples, 5 min of agitated APPJ treatment decreased total aflatoxins levels by 38% without negatively affecting chemical qualities of peanut oil (Iqdam et al., 2019). Puligundla, Lee, and Mok (2019) evaluated the effect of corona discharge plasma jet (CDPJ) treatment on the degradation of AFB<sub>1</sub> on glass slides and in spiked food samples. Following CDPJ treatment for 30 min, the AFB<sub>1</sub> concentration on slides was decreased by 95%, whereas AFB<sub>1</sub> levels in rice and wheat were only reduced by 56.6 and 45.7%, respectively. The authors suggested that this disparity could be due to chemical interaction of AFB<sub>1</sub> with the food matrix resisting the degradation of the toxin. In summary, the degradation efficiency of aflatoxins by cold plasma is highly dependent on the plasma system used, the operating parameters applied (e.g., working gas, moisture, and energy input), exposure time, and type of food products.

Clarification of the degradation mechanism with cold plasma treatment is challenging, as plasma chemistry involves hundreds of different species and thousands of possible reactions (Hertwig, Meneses, & Mathys, 2018). Wang et al. (2015b) applied ultra-performance liquid chromatography/time-of-flight mass spectrometry (UPLC/TOF-MS) to investigate the degradation products of AFB<sub>1</sub>. The addition reaction by the free radicals O<sup>•</sup> and OH<sup>•</sup> generated during RFP treatment was mainly responsible for AFB<sub>1</sub> decomposition. All the five degradation products lost their double bond in the terminal furan ring (Wang et al., 2015b). In another study, two degradation pathways of AFB<sub>1</sub> by HVACP treatment were proposed. The first pathway included several reactions in which the plasma-generated radicals, such as H<sup>•</sup>, OH<sup>•</sup>, CHO<sup>•</sup>, were joined to AFB<sub>1</sub>. The second involved epoxidation by HO<sub>2</sub><sup>•</sup> radicals and oxidation of AFB<sub>1</sub> through the combined effects of the oxidative species OH<sup>•</sup>, H<sub>2</sub>O<sub>2</sub> and O<sub>3</sub>. The decreased bioactivity of AFB<sub>1</sub> after plasma exposure was related to the loss of the double bond in difuran ring moiety, along with the modification of the lactone ring, cyclopentanone and the methoxyl group (Shi, Cooper, Stroschine, Ileleji, & Keener, 2017).

Cold plasma has been presented as a viable technology for aflatoxin decontamination in food and feed. However, this novel technology is still in the early stages of evaluation. Further research is needed to optimize plasma process conditions for different food materials. Moreover, the potential negative impacts of plasma treatment on the nutritional value and organoleptic properties of food products need to be addressed and regulated at the forefront. Finally, new plasma generating equipment, tailored for the food industry, that are easy to operate, cost effective compared with conventional approaches, and guarantee safety by adequate insulation, grounding and shielding are needed (Hertwig, Meneses, & Mathys, 2018).

### 3. Chemical degradation of aflatoxins

#### 3.1. Degradation of aflatoxins with ozone

Ozone is a powerful oxidizing agent with a redox potential of 2.07 V, capable of detoxifying a wide variety of emerging contaminants in food commodities (Pandiselvam et al., 2018). Normally, ozone can be produced by several methods such as ultraviolet irradiation, electrical discharge in oxygen and electrolysis of water (Tiwari et al., 2010). Spontaneous decomposition without forming hazardous residues on treated products makes ozone a promising alternative in food processing industry. Studies on mycotoxins degradation by ozone accelerated after it was granted Generally Recognized As Safe (GRAS) status for use in food and water (FDA, 1982; 2001). Ozonation has already been successfully employed for the removal of AFB<sub>1</sub> in laboratory-scale trials in

food, such as corn, wheat, red pepper and peanuts (Table 2). The results of sub-chronic toxicity studies on rats indicated that ozone treatment of aflatoxin-contaminated peanuts could significantly reduce hepatotoxicity and nephrotoxicity of AFB<sub>1</sub> (Diao, Hou, Chen, Shan, & Dong, 2013). The ozonolysis mechanism of AFB<sub>1</sub> involves an electrophilic attack on the double bond in difuran ring moiety, leading to the formation of a primary ozonide followed by rearrangement into molozonide derivatives such as aldehydes, ketones and organic acids (Fig. 1) (Jalili, 2016).

The ozonolysis efficiency of AFB<sub>1</sub> depends not only on ozone concentration and exposure time but also on the moisture content of the food matrix. For example, Luo et al. (2014a) observed an 88.1% reduction of AFB<sub>1</sub> in corn with 13.47% moisture content compared to a 72.4% reduction in corn with 20.37% moisture content after exposure to ozone at the concentration of 90 mg L<sup>-1</sup> for 40 min. The changes in nutritional properties of food after ozone treatment should be taken into consideration. A study conducted by Wang, King, Xu, Lasso, and Prudente (2008) showed that ozonation of naturally contaminated corn detoxified 92% of AFB<sub>1</sub> while causing a 3.2% loss in protein content. In addition, ozone was reported to change the fatty acid profile of corn (Jr. & King, 2002). However, optimization of ozone processing conditions for different food commodities to minimize its effects on quality appears to be possible. In a study of Chen et al. (2014), the conditions for degrading aflatoxins in peanuts by ozonation were optimized. A degradation rate of 65.8% was achieved in peanuts with 5% moisture content when reacted with 6.0 mg L<sup>-1</sup> of ozone for 30 min at room temperature. Meanwhile, no significant differences were found in the polyphenols, resveratrol, acid value, and peroxide value between treated and untreated samples. Most of the published reports on ozonation are based on laboratory-scale processing equipment, with a limited number of studies that focused on how to scale up the process. Hence, the successful commercial application of this technology requires the development of equipment that can efficiently eliminate aflatoxins from food and feed at high-capacity and continuous mode.

#### 3.2. Degradation of aflatoxins with electrolyzed oxidizing water

Electrolyzed oxidizing water (EOW) is generated by the passage of a dilute salt solution (~1% NaCl) through an electrolytic chamber, where the anode and cathode are separated by a membrane. The two major types of EOW are neutral electrolyzed oxidizing water (NEOW), which has a pH of 5.0–6.5, an oxidation–reduction potential (ORP) of 800–900 mV and high dissolved oxygen (DO); and acidic electrolyzed oxidizing water (AEOW), which has a pH < 3.0, a high ORP >1000 mV and high DO (Huang, Hung, Hsu, Huang, & Hwang, 2008). EOW has gained immense popularity in recent years as a novel broad-spectrum disinfectant in the food, medical and agricultural industries. EOW returns to ordinary water after use and poses no threat to humans and the environment. Chlorine and high ORP are known to be the main contributors to the sanitization effect of EOW (Rahman, Khan, & Oh, 2016). Apart from antibacterial and antifungal properties, EOW has shown promising potential for aflatoxin detoxification in agricultural products (Table 2).

Zhang, Xiong, Tatsumi, Li, and Liu (2012) observed an 85% reduction in AFB<sub>1</sub> level in peanuts after soaking for 15 min in AEOW. This treatment did not significantly affect the appearance and nutrient contents of peanuts. The AFB<sub>1</sub> degradation product following AEOW treatment was identified as AFB<sub>1</sub>-8-chloro-9-hydroxy by high-resolution Fourier transform ion cyclotron resonance mass spectrometer (HR-FT-ICR-MS) and <sup>1</sup>H nuclear magnetic resonance (<sup>1</sup>H NMR), and was determined to be devoid of mutagenicity and cytotoxicity (Xiong, Liu, & Li, 2012). In addition, the authors proposed that the high level of available chlorine concentration (ACC) in EOW was the major factor responsible for AFB<sub>1</sub> degradation, while ACC in the form of HClO was probably more efficient than ACC derived from the ionic form of ClO<sup>-</sup> in detoxifying AFB<sub>1</sub> (Zhang, Xiong, Tatsumi, Li, & Liu, 2012; Xiong, Liu, & Li, 2012). Jardon-Xicotencatl, Diaz-Torres, Marroquin-Cardona,

Table 2

Summary of recent studies (2010 to date) on aflatoxins degradation in food and feed with chemical treatments.

Treated sample	Treatment parameters	Aflatoxin ( $\mu\text{g kg}^{-1}$ or $\mu\text{g L}^{-1}$ )	Degradation (%)	Reference
<b>Ozone</b>				
Peanut	Gaseous ozone, 21 mg L <sup>-1</sup> ; Exposure for 96 h at 25 °C with flow rate of 1 L min <sup>-1</sup>	AFT (190.7)	30	(de Alencar, Faroni, Soares Nde, da Silva, & Carvalho, 2012)
Peanut	Gaseous ozone, 50 mg L <sup>-1</sup> ; Exposure for 60 h with flow rate of 5 L min <sup>-1</sup>	AFB <sub>1</sub> (189.5)	89.4	(Diao, Hou, Chen, Shan, & Dong, 2013)
Peanut	Gaseous ozone, 6.0 mg L <sup>-1</sup> ; Exposure for 30 min at room temperature	AFT (200)	65.8	(Chen et al. 2014)
Corn	Gaseous ozone, 90 mg L <sup>-1</sup> ; Exposure for 40 min	AFB <sub>1</sub> (83)	88.1	(Luo et al., 2014a)
Corn	Gaseous ozone, 75 mg L <sup>-1</sup> ; Exposure for 60 min	AFB <sub>1</sub> (53.6), AFB <sub>2</sub> (2.4) and AFG <sub>1</sub> (12.1)	86.7, 70.7 and 59.3	(Luo et al., 2014b)
Wheat	Gaseous ozone, 60 $\mu\text{mol mol}^{-1}$ ; Exposure for 3 h at 25 °C	AFB <sub>1</sub> (231.9), AFB <sub>2</sub> (265.8), AFG <sub>1</sub> (240.0) and AFG <sub>2</sub> (199.4)	94.6, 84.5, 80.0 and 81.0	(Savi, Piacentini, & Scussel, 2015)
Wheat	Gaseous ozone, 60 mg L <sup>-1</sup> ; Exposure for 5 h	AFB <sub>1</sub> (50), AFB <sub>2</sub> (50), AFG <sub>1</sub> (50) and AFG <sub>2</sub> (50)	63.2, 34.0, 54.4 and 40.3	(Trombete et al., 2017)
Poultry feed	Gaseous ozone, 5.3 mg L <sup>-1</sup> ; Exposure for 4 h at room temperature with flow rate of 1 L min <sup>-1</sup>	AFB <sub>1</sub> (32.8)	86.4	(Torlak, Akata, Erci, & Uncu, 2016)
Red pepper	Gaseous ozone, 80 mg L <sup>-1</sup> ; Exposure for 40 min	AFB <sub>1</sub> (25)	74.1	(Kamber, Gülbaz, Aksu, & Dogan, 2017)
<b>Electrolyzed oxidizing water</b>				
Peanut	AEOW: pH 2.3, ORP 1105.6 mV, ACC 71.5 mg L <sup>-1</sup> ; Soaking for 15 min at room temperature	AFB <sub>1</sub> (34.8)	85	(Zhang, Xiong, Tatsumi, Li, & Liu, 2012)
Peanut	AEOW: pH 2.5, ACC 80 to 100 mg L <sup>-1</sup> ; Soaking for 15 min at 40 °C	AFB <sub>1</sub> (95.9)	90	(Xiong, Liu, & Li, 2012)
Peanut	NEOW: pH 5.6, ACC 60 to 100 mg L <sup>-1</sup> ; Soaking for 10 min at 40 °C	AFB <sub>1</sub> (95.9)	90	

Table 2 (continued)

Treated sample	Treatment parameters	Aflatoxin ( $\mu\text{g kg}^{-1}$ or $\mu\text{g L}^{-1}$ )	Degradation (%)	Reference
Plant oils	ALEW: pH 12.2, ORP 861 mV; Soaking for 5 min at 20 °C	AFB <sub>1</sub> (40)	100	(Fan et al., 2013)
<b>Organic acids</b>				
Rice	1 N citric acid; Soaking for 15 min	AFT (86.3)	97.2	(Safara et al., 2010)
Black pepper	2% citric acid; Soaking for 2 h	AFB <sub>1</sub> (30)	29	(Jalili, Jinap, & Son, 2011)
White pepper	2% citric acid; Soaking for 2 h	AFB <sub>1</sub> (30)	28	
Soybean	1 N citric acid; Soaking at room temperature for 18 h	AFB <sub>1</sub> (7.6)	94.1	(Lee, Her, & Lee, 2015)
<b>Plant extracts</b>				
Corn	Aqueous extract of <i>Corymbia citriodora</i> leaf; Incubation at 30 °C and pH 8 for 72 h	AFB <sub>1</sub> (97.3) and AFB <sub>2</sub> (47.7)	91.7 and 88.8	(Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2015)
Corn	Aqueous extract of <i>Trachyspermum ammi</i> seed; Incubation at 30 °C and pH 8 for 72 h	AFB <sub>1</sub> (97.3) and AFB <sub>2</sub> (47.7)	89.6 and 86.5	(Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2016)
Corn	Aqueous extract of <i>Ocimum basilicum</i> leaf; Incubation at 30 °C and pH 8 for 72 h	AFB <sub>1</sub> (97.3) and AFB <sub>2</sub> (47.7)	86.9 and 83.5	(Iram et al., 2016)
Corn	Aqueous extract of <i>Allium sativum</i> , 50 $\mu\text{g mL}^{-1}$ ; Incubation at 25 °C for 1 h	AFB <sub>1</sub> (7.47)	68.3	(Negera & Washe, 2019)
Rice	Aqueous extract of <i>Ocimum tenuifloru</i> , 0.38 mg mL <sup>-1</sup> ; Incubation at 25 °C for 4 h	AFB <sub>1</sub> (1000)	42.2	(Panda & Mehta, 2013)

AFB<sub>1</sub>, Aflatoxin B<sub>1</sub>; AFB<sub>2</sub>, Aflatoxin B<sub>2</sub>; AFG<sub>1</sub>, Aflatoxin G<sub>1</sub>; AFG<sub>2</sub>, Aflatoxin G<sub>2</sub>; AFT, Total aflatoxins, the sum of AFB<sub>1</sub>, AFB<sub>2</sub>, AFG<sub>1</sub> and AFG<sub>2</sub>. AEOW, Acidic electrolyzed oxidizing water; NEOW, Neutral electrolyzed oxidizing water; ALEW, Alkaline electrolyzed oxidizing water; ORP, Oxidation-reduction potential; ACC, Available chlorine concentration.

Villarreal-Barajas, and Mendez-Albores (2015) reported that aflatoxins content in contaminated corn was not reduced following soaking in NEOW for 15 min at room temperature, as they found no difference in the aflatoxins fluorescence level of detoxified samples as compared to untreated samples. However, cytotoxicity and genotoxicity of aflatoxins in HepG2 cells were significantly reduced upon NEOW treatment. The authors further confirmed that treatment of aflatoxin-contaminated corn with NEOW effectively alleviated aflatoxicosis in turkey poult (Gomez-Espinosa et al., 2017). In order to elucidate the degradation pathway of AFB<sub>1</sub> in NEOW, Escobedo-Gonzalez et al. (2016) carried out in-silico studies by density functional theory. This analysis suggested that -Cl and -OH groups of the HOCl were added to the C8 and C9 of AFB<sub>1</sub>, yielding AFB<sub>1</sub>-8-chloro-9-hydroxy (Escobedo-Gonzalez et al., 2016).

However, it remained unclear why retention time and fluorescence strength of AFB<sub>1</sub> and AFB<sub>2</sub> in NEOW-detoxified corn did not change. In a study of Fan et al. (2013), the combination of soaking in alkaline EOW (AIEW) with pH 12.2 and oscillation at 220 rpm for 5 min was shown to completely remove AFB<sub>1</sub> in edible plant oils. The degradation of AFB<sub>1</sub> in AIEW was attributed to the reducing potential and high pH. The benefits of EOW-based food decontamination technology, including the high efficiency, low costs, and the wide range of applicability, have been highlighted in the literature (Rahman, Khan, & Oh 2016). Further evaluation of EOW application in large volumes of naturally contaminated samples is a crucial next step leading towards widespread industrial adoption.

### 3.3. Degradation of aflatoxins with organic acids

Organic acids are considered as food-grade additives by most food-safety control authorities worldwide. The degradation of aflatoxins in rice, pepper and soybeans by soaking in organic acids has been studied and proved effective in laboratory experiments (Table 2). In a study by Lee, Her, and Lee (2015), soaking of contaminated soybeans in 1.0 N citric acid, lactic acid, and tartaric acid for 18 h at room temperature reduced AFB<sub>1</sub> by 94.1, 92.7, and 95.1%, respectively. The degradation efficiency depends on temperature, moisture content, treatment time, and acid concentration. Acidulation by citric acid reduced AFB<sub>1</sub> by 97% within 96 h at room temperature, while 98% reduction was achieved by boiling AFB<sub>1</sub> for 20 min in citric acid (Rushing & Selim, 2016). Méndez-Albores, Veles-Medina, Urbina-Álvarez, Martínez-Bustos, and Moreno-Martínez (2009) evaluated the effect of extrusion-cooking process with addition of citric acid on the degradation of aflatoxins in sorghum. The result showed that the degradation rate increased with the increase of moisture content and acid concentration. Citric acid and lactic acid hydrolyzed the double bond of difuran ring moiety in AFB<sub>1</sub>, resulting in the formation of AFB<sub>1</sub>-8-hydroxy as a major degradation product (Fig. 1), which exhibited reduced toxicity on HeLa cells (Aiko, Edamana, & Mehta, 2016; Rushing & Selim, 2016). The high level of organic acids in fruit juices makes them natural and readily available sources for the degradation of AFB<sub>1</sub> in contaminated food. Rastegar et al. (2017) reported a 50.2% AFB<sub>1</sub> degradation in pistachio nuts after roasting with lemon juice at 120 °C for 60 min. Acidulation can be coupled with other techniques for synergistic effects. Abuagela et al. (2019) recently investigated the efficiency of combing acidulation followed by pulsed light treatment on aflatoxins detoxification in peanuts. This combination approach degraded aflatoxins up to 98.3%, whereas citric acid or pulsed light individually only reduced aflatoxins by 20.2 and 78.1%, respectively. Despite the leaching of nutrients like minerals, starch and water-soluble proteins into the soaking medium, changes in the chemical composition of cereal grains after soaking in organic acids may have additional benefits on the health and performance of livestock animals. Treating barley grain with 5% lactic acid has been shown to increase the content of resistant starch (RS), a functional prebiotic that can potentially stimulate hindgut fermentation and reduce the risk of metabolic diseases (Deckardt, Khiaosa-ard, Grausgruber, & Zebeli, 2014). Soaking of cereals in lactic acid can also favor the hydrolysis of phytate phosphorus, thus improving the availability of phosphorus in cereals for monogastric animals (Metzler-Zebeli, Deckardt, Schollenberger, Rodehutschord, & Zebeli, 2014; Vötterl, Zebeli, Hennig-Pauka, & Metzler-Zebeli, 2019). However, the high cost of organic acids restricts its applicability in feed manufacturing.

### 3.4. Degradation of aflatoxins with plant extracts

Natural plant extracts have been widely used as food additives and pharmaceuticals since ancient times for their anti-microbial, anti-inflammation, anti-oxidation, and immune boosting activities. The potential use of natural plant extracts in mycotoxin detoxification has received much attention in recent years. Vijayanandraj et al. (2014)

investigated aqueous extracts of 31 medicinal plants for their ability to detoxify AFB<sub>1</sub>. They found that among the different plant extracts, the leaf extract of *Adhatoda vasica* Nees showed the highest AFB<sub>1</sub>-detoxifying activity with a degradation efficiency as high as 98% after incubation at 37 °C for 24 h. The same group of researchers also demonstrated that pre-feeding rats with spray-dried formulation of *Adhatoda vasica* Nees leaf extract could counteract the hepatotoxicity induced upon subsequent exposure to AFB<sub>1</sub> (Brinda et al., 2013). In a recent study, Ponzilacqua, Rottinghaus, Landers, and Oliveira (2019) noticed a time-dependent degradation of AFB<sub>1</sub> following incubation in aqueous leaf extracts of *Rosmarinus officinalis*, with a maximum AFB<sub>1</sub> reduction of 60.3% after 48 h incubation. Moreover, some studies have demonstrated the effectiveness of natural plant extracts in eliminating aflatoxins from rice and corn as shown in Table 2. Panda and Mehta (2013) reported that a 42.2% reduction of AFB<sub>1</sub> level in rice could be achieved after incubation with an aqueous extract of *Ocimum tenuiflorum* at 25 °C. Moreover, aqueous extracts of *Corymbia citriodora* and *Trachyspermum ammi* were also studied for degrading AFB<sub>1</sub> and AFB<sub>2</sub> in contaminated corn (Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2015; Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2016). The authors found that AFB<sub>1</sub> and AFB<sub>2</sub> in spiked corn samples were degraded up to 91.7 and 88.8%, respectively, by *C. citriodora* leaf extract, while AFB<sub>1</sub> and AFB<sub>2</sub> levels were reduced by 89.6 and 86.5%, respectively, after treatment with *T. ammi* seeds extract. Mass spectrometry analysis of the degradation products confirmed that treatment with *C. citriodora* leaf extract led to lactone group modification and removal of the double bond in the difuran ring moiety of AFB<sub>1</sub> (Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2015). Similar findings were also observed after detoxification of AFB<sub>1</sub> and AFG<sub>1</sub> by *T. ammi* seeds extract (Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2016; Velazhahan et al., 2010). Brine shrimp lethality assay further confirmed much lower toxicity of degraded products compared with that of AFB<sub>1</sub> (Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2015; Iram, Anjum, Iqbal, Ghaffar, & Abbas, 2016).

Plant extracts are very complex mixtures, and their components varies with plant species and chemotype, phenological stage, tissue, and method of extraction (Figueiredo, Barroso, Pedro, & Scheffer, 2008). There has been little in-depth research to identify active compounds in plant extracts responsible for the observed detoxification of aflatoxins. A preliminary study showed that partially purified alkaloids from *Adhatoda vasica* Nees leaf extract exhibited strong AFB<sub>1</sub> detoxification activity (Vijayanandraj et al., 2014). It should also be noted that aflatoxin degradation with plant extracts could be the result of various compounds working a multi-step process. Further studies are needed to provide deeper insight into the action model as well as the potential interactions of natural plant extracts with food and feed matrices.

## 4. Biological degradation of aflatoxins

Scientists have come to favor the use of biological methods for the degradation of aflatoxins. This method takes the form of microbial or enzymatic transformation of aflatoxins into non-toxic or less toxic metabolites. A number of microorganisms from various sources such as soil, water, animal excreta and even contaminated food materials have been reported to be capable of degrading aflatoxins (Table 3). To gain further insights into microbial degradation, researchers are now focusing on the identification of functional genes and purification of aflatoxin-degrading enzymes. The use of microbes as well as isolated enzymes for the removal of aflatoxins in food and feed is an efficient, specific, and environmentally friendly decontamination strategy.

### 4.1. Microbial degradation of aflatoxins

A number of *Pseudomonas* strains, such as *P. putida* 12-3 (Elaasser & El Kassas, 2011), *P. aeruginosa* N17-1 (Sangare et al., 2014), and *P. anguilliseptica* VGF1 (Adebo, Njobeh, Sidu, Tlou, & Mavumengwana, 2016) have been reported to be capable of degrading aflatoxins. The

Table 3

Summary of aflatoxin-degrading microorganisms over the last ten years.

Microorganism	Source	Degradation condition	AFB <sub>1</sub> ( $\mu\text{g kg}^{-1}$ or $\mu\text{g L}^{-1}$ )	Degradation (%)	Reference
<b><i>Pseudomonas</i> spp.</b>					
<i>P. putida</i> 12-3	Drainage	30 °C for 72 h in cell culture supernatant	100	83.3	(Elaasser & El Kassas, 2011)
<i>P. putida</i> 1274	MTCC	30 °C for 24 h in MSG medium inoculated with cell suspensions	200	90	(Samuel, Sivaramakrishna, & Mehta, 2014)
<i>P. putida</i> 2445	MTCC	30 °C for 24 h in MSG medium inoculated with cell suspensions	200	90	
<i>P. aeruginosa</i> N17-1	Soil	37 °C for 72 h in cell culture	100	82.8	(Sangare et al., 2014)
<i>P. anguilliseptica</i> VGF1	Groundwater in gold mine	37 °C for 12 h in cell lysate	500	100	(Adebo, Njobeh, Sidu, Tlou, & Mavumengwana, 2016)
<i>P. fluorescen</i>	Groundwater in gold mine	37 °C for 12 h in cell lysate	500	100	
<b><i>Rhodococcus</i> spp.</b>					
<i>R. globerulus</i> AK36	Oil contaminated soil	28 °C for 72 h in LB medium inoculated with cell suspensions	2000	95	(Cserháti et al., 2013)
<i>R. corynebacterioides</i> JCM3376	JCM	28 °C for 72 h in LB medium inoculated with cell suspensions	2950	100	(Risa et al., 2018)
<i>R. rhodochorus</i> NI2	Hydrocarbon contaminated site	28 °C for 72 h in LB medium inoculated with cell suspensions	2000	99.1	(Krifaton et al. 2011)
<i>R. erythropolis</i> ATCC 4277	ATCC	30 °C for 24 h in Difco ISP medium No. 1 inoculated with cell suspensions	810	96	(Eshelli, Harvey, Edrada-Ebel, & McNeil, 2015)
<i>R. erythropolis</i> 4.1491	CGMCC	23.2 °C for 81.9 h in ATYP medium inoculated with cell suspensions	50	95.8	(Kong et al., 2012)
<b><i>Streptomyces</i> spp.</b>					
<i>S. lividans</i> TK 24	SIPBS	30 °C for 24 h in Difco ISP medium No. 1 inoculated with cell suspensions	810	88	(Eshelli, Harvey, Edrada-Ebel, & McNeil, 2015)
<i>S. aureofaciens</i> ATCC 10762	ATCC	30 °C for 24 h in Difco ISP medium No. 1 inoculated with cell suspensions	810	86	
<i>S. cacaoi</i> subsp. <i>asoensis</i> K234	NP	28 °C for 5 days in LB medium inoculated with cell suspensions	1000	88.3	(Harkai et al., 2016)
<b><i>Bacillus</i> spp.</b>					
<i>B. subtilis</i> ANSB060	Fish intestinal chyme	37 °C for 72 h in cell culture	100	81.5	(Gao et al., 2011)
<i>B. subtilis</i> UTBSP1	Pistachio nut	30 °C for 5 days in pistachio ground kernel inoculated with cell suspensions	2500	95	(Farzaneh et al., 2012)
<i>B. subtilis</i> JSW-1	Soil	30 °C for 72 h in cell culture supernatant	2500	62.8	(Xia et al., 2017)
<i>B. licheniformis</i> CFR1	Fallow deer faeces	37 °C for 72 h in cell culture supernatant	500	93.6	(Raksha Rao, Vipin, Hariprasad, Anu Appaiah, & Venkateswaran, 2017)
<i>B. licheniformis</i> BL010	AFB <sub>1</sub> contaminated soil	30 °C for 24 h in cell lysate	50,000	93.6	(Wang et al., 2018b)
<i>B. velezensis</i> DY3108	Soil	30 °C for 72 h in cell culture supernatant	500	82.0	(Shu et al., 2018)
<i>B. shackletonii</i> L7	Soil	37 °C for 72 h in cell culture	100	92.1	(Xu et al., 2017)
<i>B. mojavensis</i> RC3B	Pond mud	30 °C for 72 h in cell culture supernatant	179.4	75.3	(Gonzalez Pereyra, Martinez, & Cavaglieri, 2019)
<i>B. cereus</i> RC1C	Pond mud	30 °C for 72 h in cell culture supernatant	179.4	77.2	
<i>Bacillus</i> sp. TUBF1	AFB <sub>1</sub> contaminated corn	30 °C for 24 h in cell culture supernatant	10,000	100	(El-Deeb, Altalhi, Khiralla, Hassan, & Gherbawy, 2013)
<b><i>Escherichia coli</i></b>					
<i>E. coli</i> 12-5	Drainage	30 °C for 72 h in cell culture supernatant	100	62.5	(Elaasser & El Kassas, 2011)
<i>E. coli</i> CG1061	Chicken cecum chyme	37 °C for 72 h in cell culture supernatant	2500	91.9	(Wang et al., 2018a)
<b><i>Pleurotus</i> spp.</b>					
<i>P. eryngii</i> ITEM 13681	ITEM	30 °C for 28 days in corn inoculated with cell suspensions	500	86	(Brana, Cimmarusti, Haidukowski, Logrieco, & Altomare, 2017)
<i>P. ostreatus</i> GHBBF10	Decomposing tree trunk	30 °C for 15 days in rice straw inoculated with cell suspensions	500	91.8	(Das, Bhattacharya, Palaniswamy, & Angayarkanni, 2014)
<i>P. ostreatus</i> MTCC 142	MTCC	30 °C for 15 days in rice straw inoculated with cell suspensions	500	89.1	
<i>P. ostreatus</i> N001	CECT	In corn inoculated with cell suspensions	2500	91.5	(Jackson & Pryor, 2017)
<b><i>Aspergillus niger</i></b>					
<i>A. niger</i> ND-1	Feedstuff	32 °C for 24 h in culture supernatant	10	43.4	(Zhang et al., 2014)
<i>A. niger</i> FS-UV1	CCTCC	30 °C for 48 h in liquid culture of immobilized cells	50	95.3	(Sun et al., 2016)

MTCC, Microbial Type Culture Collection & Gene Bank, India; JCM, Japan Collection of Microorganism; ATCC, American Type Culture Collection; CGMCC, China General Microbiological Culture Collection Center; SIPBS, the Institute of Pharmacy and Biomedical Sciences collection at the University of Strathclyde, Glasgow, UK; ITEM, the Culture Collection of the Institute of Sciences of Food Production, Bari, Italy; CECT, Spanish Type Culture Collection; CCTCC, China Center for Type Culture Collection. NP, not provided; AFB<sub>1</sub>, Aflatoxin B<sub>1</sub>.

abilities of *P. putida* MTCC1274 and *P. putida* MTCC2445 to remove AFB<sub>1</sub> from culture medium were investigated by Samuel, Sivaramakrishna, and Mehta (2014), and the results showed that both strains of *P. putida* degraded more than 90% of AFB<sub>1</sub> during an incubation period for 24 h. Gas chromatography mass spectrometry (GC-MS) and fourier transform infrared spectroscopy (FT-IR) analyses revealed that

the lactone ring of AFB<sub>1</sub> was modified by *P. putida*, yielding three non-fluorescent compounds (AFD<sub>1</sub>, C<sub>16</sub>H<sub>14</sub>O<sub>5</sub>; AFD<sub>2</sub>, C<sub>17</sub>H<sub>14</sub>O<sub>6</sub>; and AFD<sub>3</sub>, C<sub>8</sub>H<sub>4</sub>O<sub>3</sub>). Moreover, the *in vitro* cytotoxicity test on HeLa cells showed that all these metabolites are less toxic when compared with AFB<sub>1</sub>.

A preliminary study by Cserháti et al. (2013) investigated the mycotoxin degradation ability of thirty-two *Rhodococcus* strains. The

results showed that 59% of the investigated *Rhodococcus* strains could degrade more than 90% of AFB<sub>1</sub> and remove its genotoxicity. Thin layer chromatography (TLC) analysis confirmed the cleavage of the lactone group of AFB<sub>1</sub> by *R. erythropolis* ATCC 4277 (Eshell, Harvey, Edrada-Ebel, & McNeil, 2015). Prettl et al. (2017) evaluated the potential use of *R. pyridinivorans* K408 to detoxify AFB<sub>1</sub> in corn-based whole stillage, and found that the AFB<sub>1</sub> level in solid and liquid phases of the whole stillage was eliminated by 63 and 75%, respectively.

Examination of one hundred and twentyfour *Streptomyces* strains for mycotoxin degradation showed that 55% of the *Streptomyces* strains tested were able to degrade AFB<sub>1</sub> (Harkai et al., 2016). The decrease in AFB<sub>1</sub> concentration ranged from 1.6 to 88.3%. In another work, *S. lividans* TK 24 was found to degrade 88% of AFB<sub>1</sub> in liquid culture following a 24 h incubation (Eshell et al., 2015).

Several studies have reported that *Bacillus* species can be used to degrade aflatoxins. *B. subtilis* ANSB060, isolated from fish gut, was able to degrade AFB<sub>1</sub>, AFG<sub>1</sub> and AFM<sub>1</sub> in liquid culture by 81.5, 80.7 and 60.0%, respectively, after 72 h of incubation (Gao et al., 2011). Likewise, Farzaneh et al. (2012) reported the ability of *B. subtilis* UTBSP1 to degrade up to 95% of AFB<sub>1</sub> in pistachio nuts after 5 days of treatment. In another study, it was shown that cell-free supernatant of *B. subtilis* JSW-1 had the ability to detoxify 62.8% of AFB<sub>1</sub> within 72 h (Xia et al., 2017). Several studies have also reported the degradation of AFB<sub>1</sub> by other *Bacillus* isolates, including *B. licheniformis* CFR1 (Raksha Rao, Vipin, Hariprasad, Anu Appaiah, & Venkateswaran, 2017), *B. licheniformis* BL010 (Wang et al., 2018b), *B. velezensis* DY3108 (Shu et al., 2018) and *Bacillus* sp. TUBF1 (El-Deeb, Altalhi, Khiralla, Hassan, & Gherbawy, 2013). *B. subtilis* has been approved as GRAS bacterial strains for nutritional and pharmaceutical use. Moreover, *B. subtilis* is capable of forming spores resistant to heat and low gastric pH. A commercial microbial feed additive consisting of the fermentation product of *B. subtilis* ANSB060 has been approved for commercialization in China. Most impressively, dietary supplementation of this direct-fed microbial product has been confirmed to be effective in alleviating aflatoxicosis in laying hens (Ma et al., 2012), chickens (Fan et al., 2015), ducks (Zhang et al., 2016), carps (Fan et al., 2018) and dairy cows (Guo et al., 2019).

The first evidence of the ability of *Escherichia coli* to degrade AFB<sub>1</sub> was reported by Elaasser and El Kassas (2011). In their study, culture supernatant of *E. coli* 12-5 was able to degrade 62.5% of AFB<sub>1</sub> after 72 h incubation compared to 38.3, 14.8 and 5.6% by viable cells, dead cells and cell extracts, respectively (Elaasser & El Kassas, 2011). Similarly, Wang et al. (2018a) isolated an AFB<sub>1</sub> detoxifying bacterium *E. coli* CG1061 from chicken cecum. It was found that the bacterium could degrade 93.7% of AFB<sub>1</sub> within 72 h, resulting in the formation of a range of lower molecular weight degradation products.

Previous research has also suggested the capability of some white-rot fungi from the genus *Pleurotus* to detoxify aflatoxins. The ability of *P. eryngii* ITEM 13681 to degrade AFB<sub>1</sub> under laboratory-scale mushroom cultivation was investigated by Brana, Cimmarusti, Haidukowski, Logrieco, and Altomare (2017). The mushroom growth medium contained 25% (w/w) of corn spiked with AFB<sub>1</sub> to a final concentration of 128 µg kg<sup>-1</sup>. *P. eryngii* ITEM 13681 reduced the level of AFB<sub>1</sub> in culture medium by 86% after 28 days, with no significant reduction of either biological efficiency or mushroom yield. Likewise, Jackson and Pryor (2017) found no aflatoxin residues in *P. ostreatus* mushrooms produced from AFB<sub>1</sub>-contaminated corn.

The use of non-toxicogenic *Aspergillus niger* in the food industry comes primarily from its production of various enzymes like amylase, amyloglucosidase, lactase, cellulases, pectinases, invertase, and acid proteases. Strains of *Aspergillus niger* with aflatoxin degradation ability were also selected and characterized in previous studies. Zhang et al. (2014) found that culture supernatant of *A. niger* ND-1 degraded 43.4% of AFB<sub>1</sub> after incubation at 32 °C for 24 h. In a study of Sun et al. (2016), *A. niger* FS-UV1, derived from wild strain *A. niger* FS-Z1 by mutagenic treatment with UV irradiation, displayed a superior AFB<sub>1</sub> degradation rate, reaching up to 95.3%. The results of Ames test indicated that the

mutagenic activity of AFB<sub>1</sub> was greatly abated after treatment with *A. niger* FS-UV1. Moreover, the hepatotoxicity and nephrotoxicity of AFB<sub>1</sub> in rats could be alleviated by dietary supplementation with immobilized *A. niger* FS-UV1 cells.

Microbial consortium can be constructed using bacteria, fungi or both. There are complex and intricate networks of communication in microbial communities, which play decisive role in the adaptation of microbes in the presence of xenobiotic compounds. Wang et al. (2017) developed a thermophilic microbial consortium TADC7 with stable and efficient AFB<sub>1</sub> degradation activity. Cell-free supernatant of TADC7 consortium showed AFB<sub>1</sub> degradation rate of more than 95% in a wide temperature range from 50 to 90 °C. According to 16S rDNA sequencing analysis, *Geobacillus* and *Tepidimicrobium* may play major roles in AFB<sub>1</sub> degradation by TADC7 consortium.

#### 4.2. Enzymatic degradation of aflatoxins

Important technological advances in the field of molecular biology have allowed scientists to isolate and identify aflatoxin-degrading enzymes from microbes. A schematic diagram describing the workflow of research on aflatoxin-degrading enzymes is shown in Fig. 2. Biodegradation based on cell-free enzyme preparations avoids the shortcoming of applying whole microorganisms, which apart from their degradation activity, may impair the organoleptic properties of food commodities and produce undesirable compounds (Adebo, Njobeh, Gbashi, Nwinyi, & Mavumengwana, 2017). Previous studies have documented that aflatoxins could be degraded by laccases, peroxidases, oxidases and reductases. The reaction mechanisms for AFB<sub>1</sub> detoxification catalyzed by aflatoxin-degrading enzymes are summarized in Fig. 3.

Laccases are a class of blue multicopper enzymes capable of oxidizing a wide variety of phenolic and non-phenolic aromatic compounds while reducing molecular oxygen in water. Laccases are widespread in nature, occurring in bacteria, fungi, higher plants and insects. The use of fungal laccases in AFB<sub>1</sub> decontamination was first proposed by Alberts, Gelderblom, Botha, and van Zyl (2009). The research group successfully employed pure laccase from *Trametes versicolor* and a recombinant laccase produced by *A. niger* to degrade AFB<sub>1</sub>. The treatment of AFB<sub>1</sub> with *T. versicolor* laccase resulted in a 59% reduction in pro-oxidative properties and complete elimination of genotoxicity (Zein-vand-Lorestani et al., 2015). The catalytic capacity of laccase enzyme can be greatly improved by combining it with redox mediators, which serve as electron shuttles between laccase and target substrate. The AFB<sub>1</sub> degradation by Lac2 laccase from *Pleurotus pulmonarius* was remarkably enhanced by 23 to 99% with the addition of 10 mM acetosyringone (AS) as a redox mediator (Loi et al., 2016). Oxidation of AFB<sub>1</sub> following 72-h incubation with Ery4 laccase from *Pleurotus eryngii* was evaluated in the presence of eight different redox mediators. The results showed that syringl-type phenols acetosyringone (AS) and syringaldehyde (SA) were the best performing mediators with degradation percentages of 73 and 68%, while hydroxybenzotriazole (HBT), phenol red (PhR) and 2, 2, 6, 6-tetramethylpyridyloxil (TEMPO) were less or totally non-efficient in AFB<sub>1</sub> degradation (Loi et al., 2018). Compared with fungal laccases, bacterial laccases exhibit notable features of high thermostability, wide pH range, broad substrate spectrum and tolerance to alkaline conditions (Guan, Luo, Wang, Chen, & Liao, 2018), which make bacterial laccases excellent candidates for the degradation of xenobiotics. Recently, Guo et al. (2020) reported that *B. licheniformis* CotA laccase could catalyze the C3-hydroxylation of AFB<sub>1</sub>, and the transformation products aflatoxin Q<sub>1</sub> and epi-aflatoxin Q<sub>1</sub> were non-toxic to human liver cells L-02. The CotA laccase was highly thermostable with a half-life of 1 h at 70 °C, and the enzyme could degrade more than 70% of AFB<sub>1</sub> in temperature range from 60 to 80 °C within 30 min. Molecular docking simulation predicted that AFB<sub>1</sub> interacted with CotA laccase through hydrogen bonding and van der Waals interaction.

Peroxidases represent a large family of oxidoreductase enzymes that can catalyze the oxidation of various electron donor substrates with the

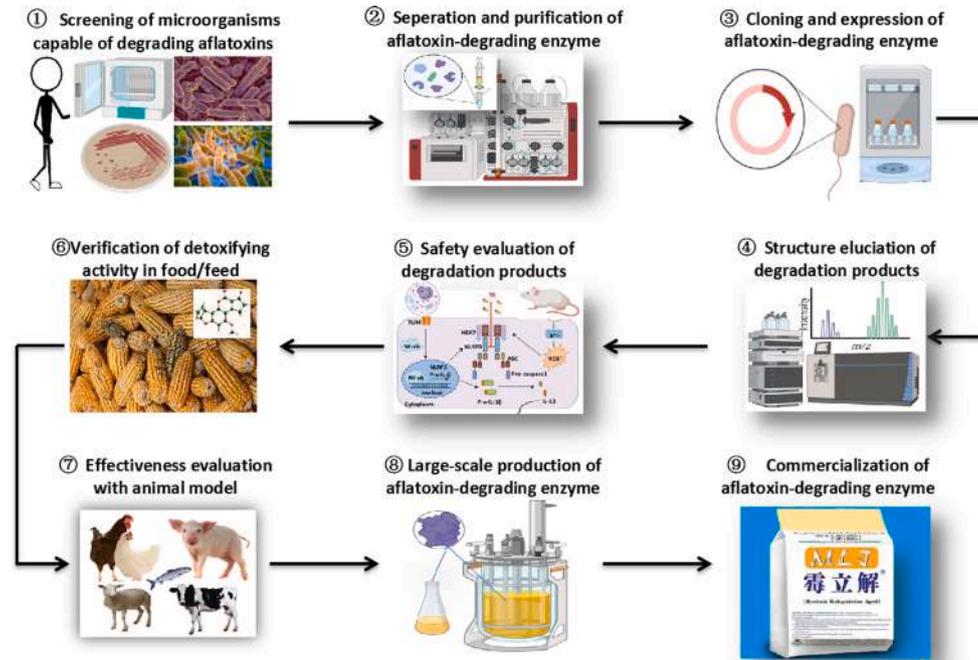


Fig. 2. Workflow of research on aflatoxin-degrading enzymes.

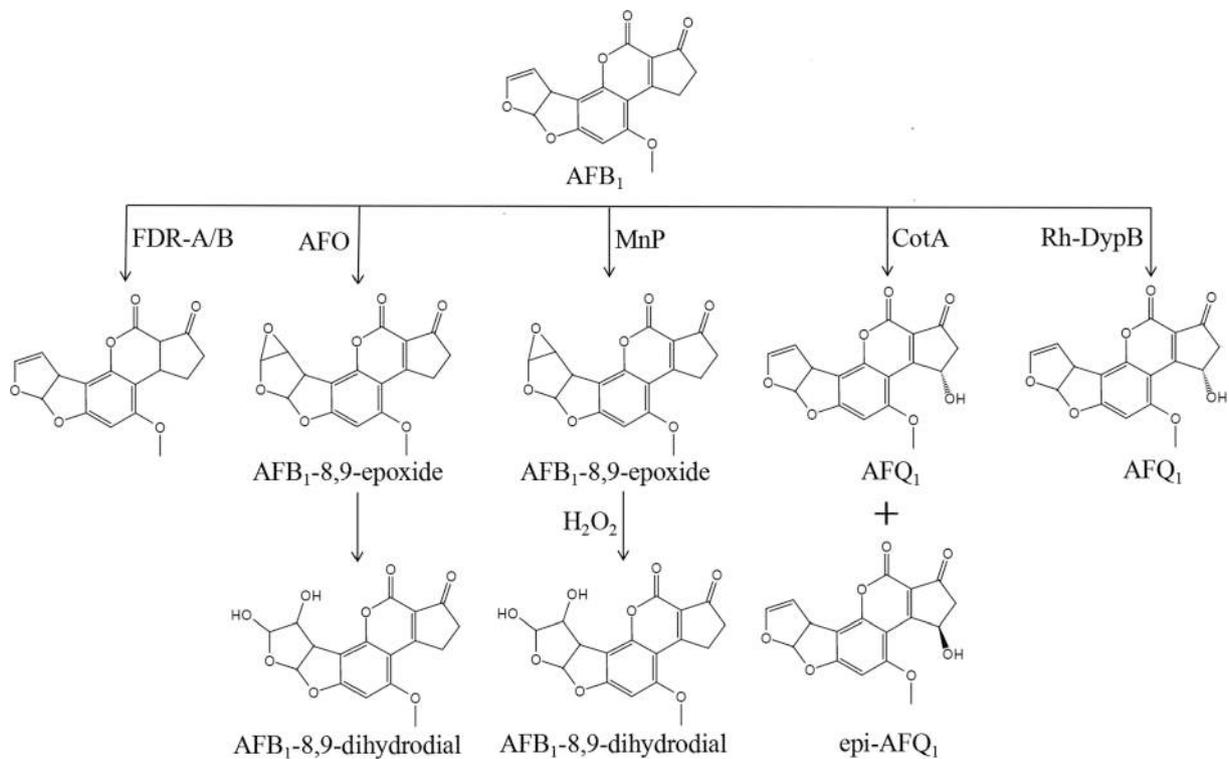


Fig. 3. The degradation pathways of AFB<sub>1</sub> by aflatoxin-degrading enzymes.

concomitant decomposition of H<sub>2</sub>O<sub>2</sub>. A vast majority of peroxidases are heme-containing and ubiquitously present in prokaryotes and eukaryotes. Enzymatic degradation of aflatoxins by peroxidases derived from various sources has been reported. Das and Mishra (2000) achieved a 53% AFB<sub>1</sub> reduction in groundnut meal by using horse radish peroxidase (HRP). In addition, Marimón Sibaja et al. (2018) reported that HRP reduced AFB<sub>1</sub> and AFM<sub>1</sub> levels by 97 and 65%, respectively, in milk after 8 h at 30 °C. In a study of Tripathi and Mishra (2009), a 70% degradation

of AFB<sub>1</sub> in red chili powder was observed upon treatment with garlic peroxidase for 30 h. Wang, Ogata, Hirai, and Kawagishi (2011) examined the ability of manganese peroxidase (MnP) from white-rot fungus *Phanerochaete sordida* YK-624 in degrading AFB<sub>1</sub>. The study showed that the enzyme was able to degrade 86.0% of AFB<sub>1</sub> and reduced its mutagenic activity by 69.2%. Based on <sup>1</sup>H NMR and high resolution electrospray ionization mass spectrometry (HR-ESI-MS) analysis, the authors proposed that AFB<sub>1</sub> was first oxidized to an epoxide

intermediate AFB<sub>1</sub>-8, 9-epoxide by MnP, and then hydrolyzed to AFB<sub>1</sub>-8, 9-dihydrodiol accompanied by H<sub>2</sub>O<sub>2</sub> addition (Wang, Ogata, Hirai, and Kawagishi, 2011). Furthermore, Wang et al. (2019) revealed that AFB<sub>1</sub> degradation by MnP was achieved by free radical attack, which shared the same mechanism of MnP-mediated dye decolorization. The rate of AFB<sub>1</sub> degradation by different MnPs was positively related to their ability to decolorize reactive black 5. As a new family of microbial peroxidases, dye-decolorizing peroxidases (DyP) were named for their ability to efficiently oxidize synthetic anthraquinone and azo-dyes. Loi et al. (2020) recently reported that the type B dye decolorizing peroxidase (Rh\_DypB) from *Rhodococcus jostii* could degrade up to 96% of AFB<sub>1</sub> in sodium malonate buffer, resulting in the formation of AFQ<sub>1</sub> as major transformation product.

Liu et al. (1998; 2001) isolated and purified an aflatoxin detoxifying enzyme (ADTZ) from the mushroom *Armillariella tabescens*. The enzyme was subsequently identified and renamed aflatoxin oxidase (AFO) (Cao, Liu, Mo, Xie, & Yao, 2011). Bioinformatic analysis showed that AFO shared 42% amino acid sequence similarity with dipeptidyl peptidase III (DPP III), a zinc-dependent hydrolase from M49 family of metalloproteases (Wu et al., 2015). Further investigation confirmed that AFO was a dual activity enzyme with both aflatoxin-oxidase and dipeptidyl peptidase activities (Xu, Xie, Yao, Zhou, & Liu, 2017). AFO was also able to act on versicolorin A, 3, 4-dihydro-2H-pyran and furan which shared the structure of furan or pyran ring with AFB<sub>1</sub>, indicating that double bond in difuran ring moiety of AFB<sub>1</sub> was the potential action site for AFO (Wu et al., 2015). During this reaction, H<sub>2</sub>O<sub>2</sub> was produced with water as the hydrogen donor (Wu et al., 2015). It was worth noting that Guan and colleagues successfully expressed AFO in the parotid gland of mice and pigs, and confirmed that AFO in the saliva could effectively eliminate the toxicity of AFB<sub>1</sub> in transgenic mice and pigs (Guan et al., 2015; Lou et al., 2017). These findings pave a new way for the application of aflatoxin-detoxifying enzyme gene in breeding animal species with aflatoxin resistance.

Taylor et al. (2010) identified and characterized nine F<sub>420</sub>H<sub>2</sub>-dependent reductases (FDRs) from *Mycobacterium smegmatis* that utilized the deazaflavin cofactor F<sub>420</sub>H<sub>2</sub> to catalyze the reduction of the  $\alpha$ ,  $\beta$ -unsaturated ester moiety of aflatoxins. These enzymes fall into two classes (FDR-A and -B), and the class of FDR-A enzymes has up to 100 times more activity than the FDA-B class (Lapalnikar et al., 2012). In a recent investigation, Li et al. (2019) showed that DNA damage and p53-mediated apoptosis in HepG2 cells exposed to AFB<sub>1</sub> could be significantly reduced by the addition of the recombinant FDR-A enzyme MSMEG-5998 in culture medium.

Academics have been working continuously to explore novel aflatoxin-degrading enzymes. Zhao et al. (2011) purified a 32 kDa extracellular enzyme MADE from *Myxococcus fulvus*. The optimum condition for the AFB<sub>1</sub>-degrading activity of MADE was observed at pH 6.0 and 35 °C. The purified MADE could also degrade AFM<sub>1</sub> and AFG<sub>1</sub> by 96 and 97% after 48 h of incubation. Similar studies on a purified enzyme BADE from *Bacillus shackletonii* showed that the enzyme was able to degrade 48% of AFB<sub>1</sub> at 70 °C after 72 h (Xu et al., 2017). Importantly, BADE was highly thermostable and retained its activity after boiling at 100 °C for 10 min. The authors speculated that BADE was an oxidoreductase that utilized copper ion as an activator. The AFB<sub>1</sub>-degrading activity of BADE was significantly improved in the presence of copper ion. However, the amino acid sequences of MADE and BADE have not been reported. In a more recent study, Xie, Wang, and Zhang (2019) isolated a 38 kDa AFB<sub>1</sub>-degrading enzyme PADE from *Pantoea* sp. T6, which was matched to the outer membrane protein A (OmpA) in the Uniprot database (Accession No. A0A1X1BYP1) by peptide mass fingerprint analysis. The catalytic function of OmpA has not been reported in previous studies. Further investigation is required to understand the AFB<sub>1</sub> degradation activity of *Pantoea* sp. T6 OmpA.

While these aflatoxin-degrading enzymes are effective, there are practical obstacles to their application in food and feed industry. One of the main problems is the low production yields of these enzymes in their

native hosts. Thus, it would be economically unfeasible to produce them using standard fermentation or culture techniques. However, production of these enzymes using recombinant DNA technologies could address this issue. On the other hand, modern food and feed processing tends to be sophisticated and precise, and generally requires high temperature, extreme pH, and the use of solvents (Zhang, Geary, & Simpson, 2019). However, the stability and catalytic efficiency of wild-type enzymes under stress conditions is less than satisfactory. The recently developed enzyme engineering technologies like random mutagenesis and directed evolution will open the gate to the improvement of properties of aflatoxin-degrading enzymes. Biological agents to be used in practice as animal feed additives must rapidly degrade mycotoxins into non-toxic metabolites, under different oxygen conditions and in a complex environment (Boudergue et al. 2009). Up to now, there is still lack of scientific methods standardized to investigate the activity of mycotoxin-degrading enzymes in the digestive systems of animals. *In vitro* models mimicking the digestive process in the gastric-intestinal tract have been proposed to assess the effects of different feed enzymes (phytase, xylanase, and  $\beta$ -glucanase) on release of trace elements in feedstuffs (Yu, Han, Li, Zhang, & Feng, 2018). Thus, it is possible to develop *in vitro* models to evaluate the efficiency of aflatoxin-degrading enzymes in reducing the bioavailability of aflatoxins in the digestive tract of animals.

## 5. Future perspective of nanozymes in aflatoxins degradation

Given the diverse nature of the food and feed industry, there is the need for the development of novel technologies for sustainability, safety, profitability, and to gain consumer trust (Pal et al., 2016). Nanozymes refer to nanomaterials with enzyme-mimicking activity, which can catalyze the conversion of substrates and follow the same kinetics and mechanisms as natural enzymes under physiological conditions (Wei & Wang, 2013). Since the discovery of Fe<sub>3</sub>O<sub>4</sub> nanoparticles with intrinsic peroxidase-like activity in 2007 (Gao et al., 2007), a large number of studies on nanozymes have emerged. Compared with natural enzymes, nanozymes show better stability and durability due to the inherent properties of nanomaterial. Inspired by the structure of the active site and the electron transfer pathway of laccases, Liang et al. (2017) prepared a laccase-mimicking nanozyme by coordinating guanosine monophosphate (GMP) with Cu<sup>2+</sup> to form amorphous metal-organic framework (MOF) nanomaterial. The preparation of Cu/GMP nanozyme is very simple with a mixture of two common chemicals at room temperature. The Cu/GMP nanozyme is about 2400-fold more cost-effective than commercial protein laccase in achieving the same catalytic efficiency. Moreover, the Cu/GMP nanozyme is robust against extreme pH, temperature, salt, and long-term storage. Considering that both bacterial and fungal laccases exhibit AFB<sub>1</sub> oxidation capacity, it is of great interest to evaluate the potential use of this Cu/GMP nanozyme in AFB<sub>1</sub> removal.

Up to now, several nanomaterials with peroxidase-like activity have been constructed such as Pt<sub>74</sub>Ag<sub>26</sub> nanoparticle-decorated ultrathin MoS<sub>2</sub> nanosheets (Cai et al., 2016), FePt nanoparticle-decorated graphene oxide nanosheets (Chen et al., 2018), FeMnO<sub>3</sub> nanoparticle-filled polypyrrole nanotubes (Chi, Chen, Zhong, Wang, & Lu, 2018), and CuMnO<sub>2</sub> nanoflakes (Chen, Chen, Wu, & Yang, 2019). An interesting attempt was made by Ren, Luo, and Wan (2019) using peroxidase-like Fe-based MOFs for the degradation of AFB<sub>1</sub>. The MOFs was able to degrade more than 85% of AFB<sub>1</sub> at the initial concentration of 50  $\mu$ g mL<sup>-1</sup>. Corn starch, corn oil and cellulose have little impact on the ability of peroxidase-like catalytic system to degrade AFB<sub>1</sub>. The hepatotoxicity of AFB<sub>1</sub> is detoxified by peroxidase-like MOFs as AFB<sub>1</sub> is transformed into a variety of low-carbon compounds. H<sub>2</sub>O<sub>2</sub> is required for peroxidase-catalyzed degradation of xenobiotic compounds. With molecular oxygen as an electron acceptor, glucose oxidase (GOx) can catalyze the oxidation of  $\beta$ -D-glucose to D-glucono- $\delta$ -lactone and H<sub>2</sub>O<sub>2</sub>, which is an easy way to generate H<sub>2</sub>O<sub>2</sub> in food commodities. Thus, the GOD and peroxidase cascade reaction could be an ideal strategy for

degrading AFB<sub>1</sub> in real food systems. Hou et al. (2015) developed a mimetic multi-enzyme system by embedding GOx in a mimetic peroxidase zeolitic imidazolate framework 8 (mZIF-8), which showed highly catalytic activity and sensitivity to glucose, and the produced H<sub>2</sub>O<sub>2</sub> could be immediately decomposed by the support mZIF-8 to oxidize o-phenylenediamine. Moreover, the mZIF-8@GOx exhibited excellent reusability, retaining about 88.7% residual activity after 12 times reuse. These research advances will pave the way for the development of nanzyme-based antidotes to aflatoxins in the coming years.

## 6. Conclusion

Aflatoxin contamination in agricultural commodities is of worldwide concern, both for its negative impacts on human and animal health and the considerable economic loss to the food and feed industry. The growing consumer demand for safe and high quality food has driven scientists to develop effective degradation technologies for this carcinogenic food contaminant. Despite the intensive research in this field and of the numerous publications that show the success of various physical, chemical and biological approaches, the results achieved till date can only be considered as the first step in the development of commercially feasible technologies. Several criteria must be met by methods suitable for industrialization: (1) effectively and rapidly reduce aflatoxins to acceptable levels; (2) not produce or leave toxic residues in food and feed; (3) retain the nutritive value and sensory properties of food and feed; (4) be economically feasible and environmentally friendly; and (5) if possible, destroy fungal spores. Studies involving irradiation and cold plasma have led to encouraging outcomes, but the majority of experiments are performed in model systems and in laboratory conditions. The applicability of ozone, electrolyzed oxidizing water, organic acids and plant extracts depends not only on their efficacy and safety, but also on consumer acceptance. In our opinion, biodegradation using probiotics as well as isolated enzymes has good potential for large-scale applications. A number of studies have confirmed both *in vitro* and *in vivo* detoxification capacity of probiotic *Bacillus* species, which can be directly incorporated into feed to protect farm animals from aflatoxicosis. Fermented food products have a long tradition in Southeast Asia where there is remarkable market opportunity for aflatoxin-free fermented food by using aflatoxin-degrading probiotics as fermenting microbes. Many enzymes such as protease, amylase, lipase, phytase, glucose oxidase and others have been successfully applied in the food and feed industry. Thus, the adoption of cost-effective aflatoxin-degrading enzymes with high efficiency and specificity for post-harvest aflatoxin decontamination can be expected in the near future.

## CRedit authorship contribution statement

**Yongpeng Guo:** Investigation, Data curation, Writing - original draft. **Lihong Zhao:** Supervision, Writing - review & editing, Funding acquisition. **Qiugang Ma:** Validation. **Cheng Ji:** Visualization.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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