ajfand AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

Afr. J. Food Agric. Nutr. Dev. 2024; 24(3): 25851-25870 https://doi.org/10.18697/ajfand.128.24315

Date	Submitted	Accepted	Published
	30th October 2023	12th March 2024	6th April 2024

REVIEW ON NOVEL APPROACHES FOR CONTROLLING AFLATOXIN B1: HARNESSING NATURE'S DEFENSES AGAINST FOOD TOXINS

Fossou JPM[1,2], Adjovi YCS[1,2*], Dedehou SE[1,2], Ahehehinnou UH[1,2] and F Tovo[1]

Yann Christie Sissinto Adjovi

*Corresponding author email: yann.adjovi6@gmail.com

[1]Laboratoire de Biochimie et de Biologie moléculaire, Centre Béninois de la Recherche Scientifique et de l’Innovation, Cotonou, Bénin

[2]Université Nationale d’Agriculture, Porto-Novo, Bénin

ABSTRACT

Aflatoxin B1 is the most harmful food toxin for humans and animals. According to the International Agency for Research on Cancer, it is ranked as one of the most carcinogenic substances in the world, directly connected to hepatocarcinoma in both humans and animals. Aflatoxin B1 is also involved in the occurrence of pathologies, and aflatoxicoses. Aflatoxin B1 can be produced by fungi from the genus *Aspergillus* section *Flavi* in a variety of foods during storage. Once aflatoxins are present, food processing cannot eradicate them. The damage and lack of complete elimination of aflatoxins from foodstuffs make them the most monitored and controlled substances in the world. Given the high-risk of Aflatoxin B1 on both animal and human health, it is important to study their worldwide distribution and existing control methods through a systematic review. Articles published from 1945 to 2022 found on several databases as Scopus, PubMed, Dimensions, Google Scholar and an extraction sieve was used to select the relevant articles. Of the two hundred and twenty-eight (228) French and English scientific articles on aflatoxins identified, forty of the most relevant original articles were selected for inclusion in this review following a rigorous selection process. Several genes are involved in the synthesis of aflatoxin B1. Moreover, certain environmental conditions, in particular oxidative stress are propitious for fungus by over-expressing aflatoxins. However, the fungi defences can be controlled by several methods. Articles showed efficiency of various of them. Good cultural practices and awareness raising are part of the preventive control. Synthetic chemicals such as insecticides and fungicides are chronically used in chemical control of fungal growth and prevent aflatoxins from being produced. Biological control is based on allelic recombination between toxic and atoxic strains. The use of microbial competition is focused on the natural predators of aflatoxic molds, most often lactic acid bacteria, and the natural control relies on the use of natural plant substances. Natural substances like aqueous or organic plant extracts that contain proteins, polyphenols, tannins, antioxidants, flavonoids, terpenes, and chelating ion as well as caffeic acid, gallic acid and ascorbic acid can be used to control fungal contamination currently. These molecules interfere with free radicals to slow down or even inhibit the production of reactive oxygen species significantly reducing the production of aflatoxins making them inactive. Implementation of the means of controlling fungal growth and producing aflatoxins will help make agriculture globally competitive and ensure food security.

Key words: Natural substances, Aflatoxin B1, food poisoning, alternative control, biocontrol

INTRODUCTION

Since the first cases of acute aflatoxicosis known as turkey X disease in 1960, involving the death of turkey poults, the Tropical Products Institute in London and the Central Veterinary Laboratory in Meybridge have shown the direct involvement of *Aspergillus flavus* and its toxins known as "aflatoxins" in the death of these animals [1]. Then, the first case of human aflatoxicosis, in a young Ugandan, was reported by Diom (1978). This young man suffered from hepatic necrosis after eating food heavily contaminated with aflatoxins.

In 1945, Hintermann and Ninard [2] had already implicated the diet of pigs that had died from eating oilcake and whose livers showed necrotising and tumourous liver lesions at autopsy. Since then, a great deal of research has focused on the contamination of foodstuffs by Aspergilli and their toxins, the risks they could present to humans and livestock, and ways of controlling poisoning.

Declared a carcinogenic substance by the International Agency for Research on Cancer in 2002 [3], aflatoxin B1 is one of the most closely monitored and regulated toxins in the world [4] due to its ubiquity in all major [5] and the impossibility of a total ban. Despite their proven effectiveness, the use of conventional and traditional methods of combating fungal development and toxin synthesis through the repeated use of non-selective or poorly selective broad-spectrum plant protection products is highly problematic. They have potentially harmful effects on biodiversity, with the emergence of resistance [6], food poisoning and the risk of pathologies [7, 8].

These observations, together with the growing awareness of public policies, are motivating the search for new, innovative methods of preventing fungal attacks. These methods involve the use of natural substances extracted from plants and microbial competitions to ensure the preservation of cereals during storage. This paper, therefore, summarises the work that has been carried out on alternative control methods against aflatoxins and aflatoxigenic fungi, as well as the various techniques for controlling the aflatoxin synthesis process and the prospects for more responsible control that respects the environment and human, animal and plant populations.

In Africa, Partnership for Aflatoxin Control in Africa [9] states that aflatoxins contribute greatly to the impoverishment of African populations, not only because of the heavy economic losses they cause, but also because of their direct involvement in the development of liver cancer, hepatic and immune diseases and stunted growth in children. These toxins are produced by fungi in general and the genus *Aspergillus* section *Flavi* in particular. They are formidable food contaminants and a major danger to the general public. From 1960 to the present

ajfand AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

day, numerous studies have revealed that agricultural products and other foodstuffs grown and marketed around the world are heavily contaminated by aflatoxins. This work therefore wanted to take stock of the conditions under which aflatoxins are biosynthesised, the most contaminated agricultural products and the alternative methods of control suggested by the results of relevant research.

MATERIALS AND METHODS

Selecting and filtering articles

An extraction sieve was used to select the relevant scientific articles and reports from international organizations. This sieve consisted of a multi-level scientific approach, as shown in Figure 1.

https://doi.org/10.18697/ajfand.128.24315

ajfand
AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

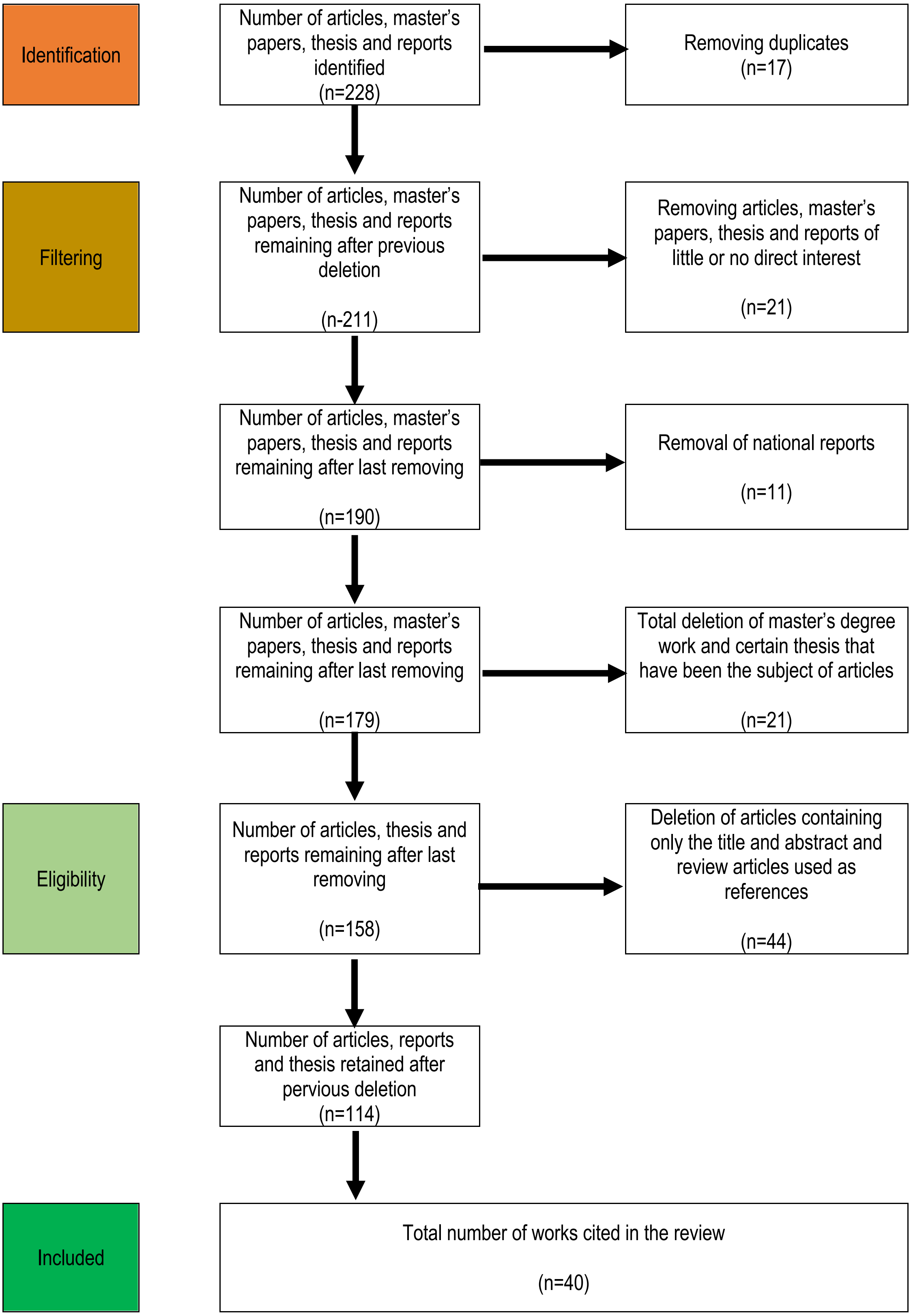

Figure 1: Methodological diagram for selecting the articles used

ajfand AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

RESULTS AND DISCUSSION

Nomenclature of research used

By applying the inclusion and exclusion criteria, around forty relevant scientific works, as shown in Figure 2 below.

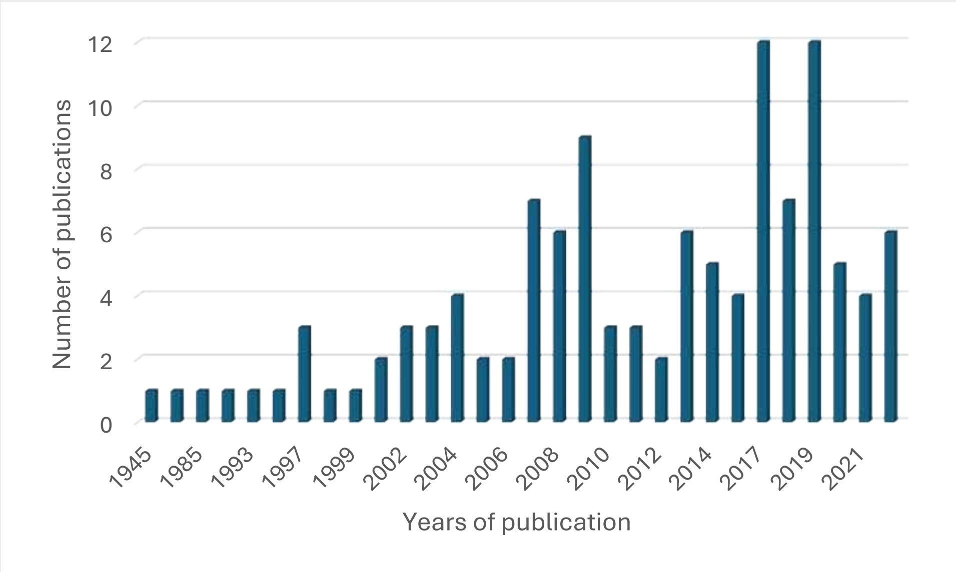

Figure 2: Histogram of scientific works consulted

All countries are concerned with the risks associated with aflatoxin contamination of foodstuffs and animal feedstuffs. The work consulted in this review is the result of research carried out in different parts of the world, as shown in Figure 3.

https://doi.org/10.18697/ajfand.128.24315

ajfand
AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

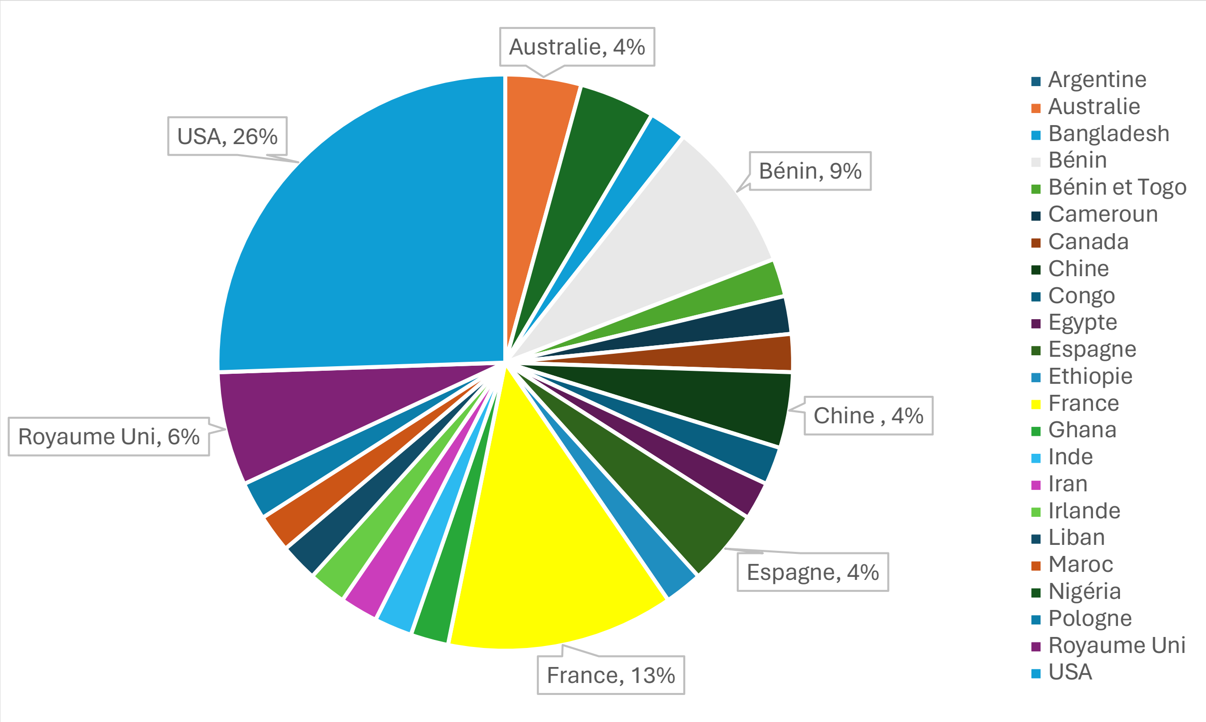

Figure 3: Worldwide distribution of scientific works consulted

Aflatoxigenic fungi and aflatoxin biosynthesis

Aspergillus flavus is one of 16 aflatoxigenic species out of the 33 species in the *Flavi* section [10]. All other aflatoxigenic strains are derived from *A. flavus* [11]. Along with *A. parasiticus*, *A. flavus* are attracting more attention because they are not only pathogenic for certain plants but also produce aflatoxins [12]. Mycotoxins constitute the large group of toxic substances produced by different fugal strains, including aflatoxins.

The mycotoxin content of a substrate is not proportional to its degree of fungal contamination [13]. Several conditions, particularly environmental are, therefore, essential for the production of mycotoxins. Fungi proliferation and aflatoxin production depend on the presence of spores, an appropriate temperature, a food source (organic substrate) and humidity [14]. Fungal contamination is particularly pronounced in tropical and subtropical regions where hydrothermal conditions such as water activity (aw=0.65), temperature around 33°C, pH, humidity and latitude are favourable to fungal development and toxin production [10]. With regards to temperature, Diom [1] reported that production of aflatoxins B1, B2, G1 and G2 was, respectively, 40, 10, 13 and 4 times higher at 30°C than at 20°C after nine (09) days [1]. These results are confirmed by Giorni [15], who established the link between high temperatures and increased fungal and aflatoxic contamination of maize in Italy. Increased fungal contamination increases the risk of mycotoxin production throughout the food chain (field, storage, processing) [16].

ajfand AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

Other conditions such as storage time, degree of ripening, cross-contamination, the presence of aflatoxigenic fungi, insects, physical damage to grains, harvesting technique and storage premises can contribute to fungal proliferation [13]. Heat and drought are other factors that stimulate fungal development and aflatoxin production [11].

Substrates have a major influence on aflatoxin production [17]. Optimal aflatoxin production is observed in groundnuts [1, 17]. The substrates most likely to be contaminated are peanuts, cereals and certain spices such as red pepper [14]. These results confirm those of Negash [11] on the presence of high levels of aflatoxin B1 in groundnuts and maize in Ethiopia and also those of Gnonlonfin *et al.* [18] who showed that spices marketed in southern Benin and Togo were heavily contaminated by toxinogenic *Aspergillus* species with high production of aflatoxin B1 in garlic and ginger and to a lesser extent in pepper. In addition, cassava chips [19] and smoked, fermented or dried fish sold in the main markets of Cotonou (Benin) are choice substrates for *A. flavus* [20].

Aflatoxins are highly toxic toxins, carcinogenic [3] immunosuppressive and teratogenic [22], and lethal, discovered in England during the turkey epidemic. The most toxic type, aflatoxin B1, is directly linked to liver cancer [7]. A direct link has been established between the structure of AFB1 and its high toxicity [23]. Hydrogenation of the double bond on the furfurol ring reduces toxicity [1]. This hydrogenation is absent from the furfurol nucleus of AFB1, making it 10 times more toxic than AFG2. The complexity of aflatoxin biosynthesis also contributes to their toxicity [7]. For Ehrlich and Yu [7], the conversion step from versicolorin A (VHA) to versicolorin B (VHB) determines the high toxicity and carcinogenicity of aflatoxins. Exposure to aflatoxins occurs mainly through ingestion of contaminated food [13], inhalation of conidia or via the skin [24] (Figure 4). Their toxicity varies depending on the species and age of the animals [1]. Some animals, such as pigs, ducks and turkeys, are more sensitive than chickens, sheep or mice. After entering the body, AFB1 enters the bloodstream and is then found in the liver, its main target, where it is metabolised. In the liver, aflatoxin B1 is metabolised by three (03) completely different metabolic pathways (Figure 5).

ajfand
AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

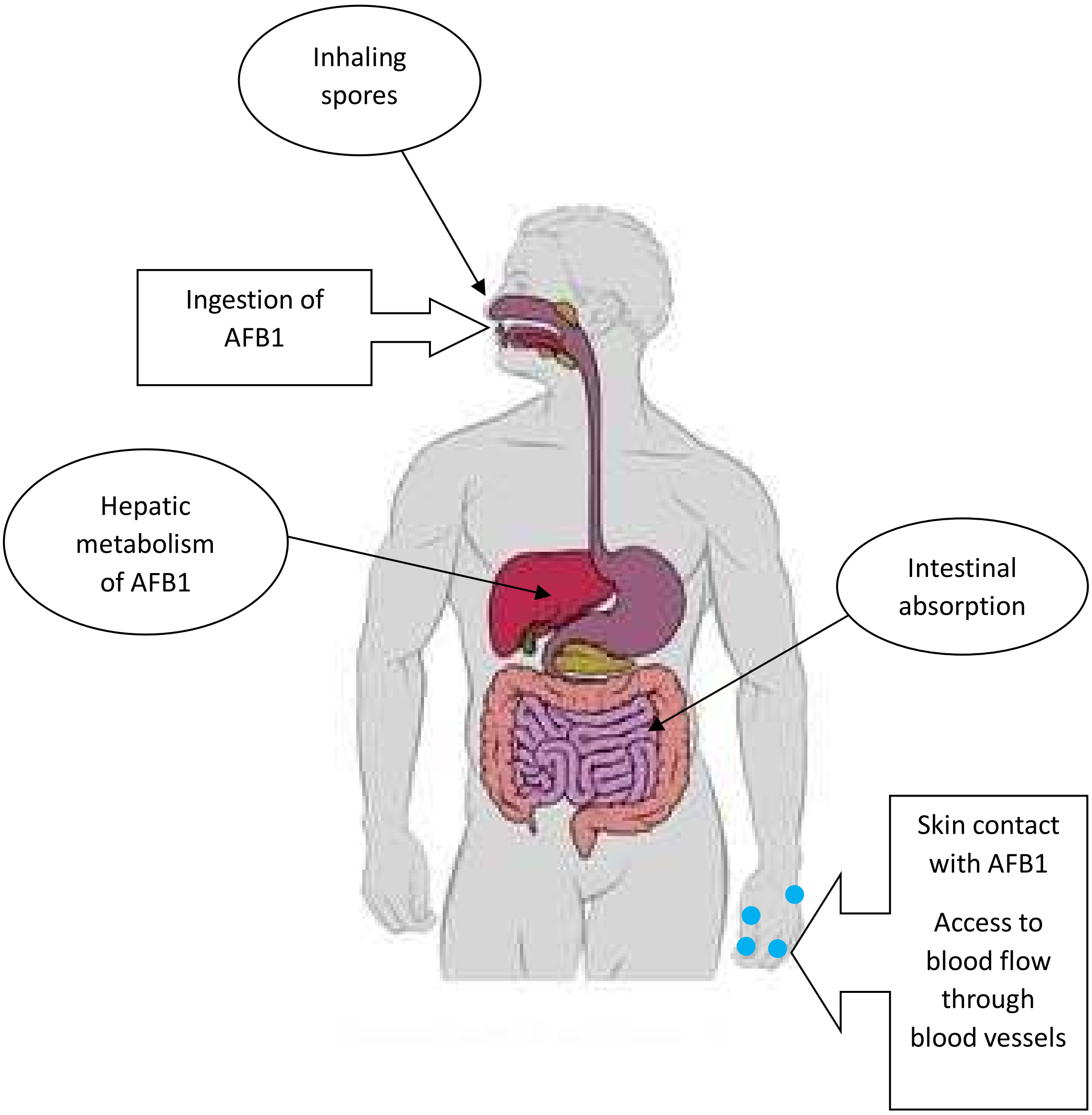

Figure 4: AFB1 uptake pathways

ajfand
AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

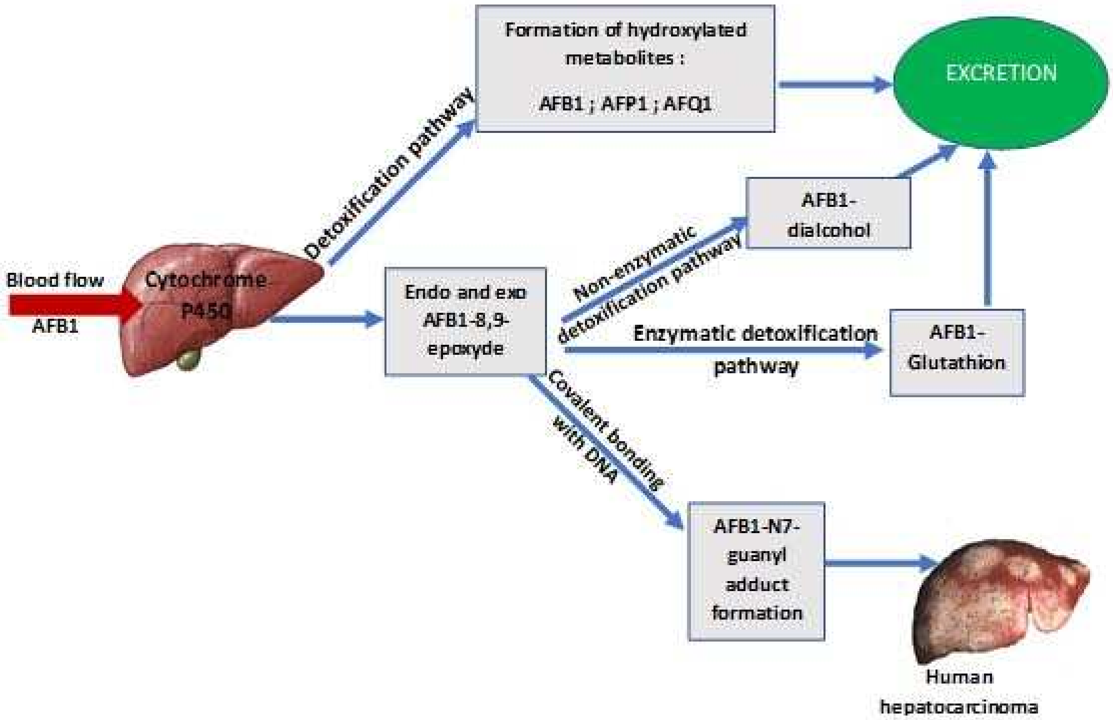

Figure 5: Different metabolic pathways of AFB1

Aflatoxin is a stable molecule that is highly resistant to various food processing methods such as extrusion, cooking and even roasting [21]. In fact, aflatoxins break down at very high temperatures of between 237 and 306°C [25], which is difficult to reconcile with traditional food manufacturing or processing methods. For example, AFG2 is denatured from 237°C, AFG1 breaks down between 244 and 246°C, while AFB1 and AFB2 prove to be even more resistant, they decompose between 268-269° and 286-289°C, respectively [26]. The preventive method therefore remains the only alternative.

Control methods

The control of aflatoxin biosynthesis, particularly aflatoxin B1, by chemical compounds and natural plant substances can be very effective. Blocking the enzymatic system developed by the fungi can offer an alternative way of inhibiting aflatoxin production. Numerous studies, have shown that this control can be achieved using several natural substances such as antioxidants, phenolic compounds (tannins, flavonoids), alkaloids, gallic acid and caffeic acid extracted from plants [26,27,28].

Preharvest and harvest management

Aflatoxins are the most dangerous toxins found in food. They are highly resistant to heat treatment and are found in food after cooking [26]. In Benin, high concentrations of aflatoxins have been found in 'adoyo', a drink made from maize

[29]. Far from being an isolated case, Bailly *et al.* [10] reports high concentrations of aflatoxin M1 in milk just about everywhere in Europe, while another study found it in coffee and tea and even in roasted coffee [30]. To control aflatoxin contamination and mitigate its persistence, the Partnership for Aflatoxin Control in Africa proposed in 2017 a strategy for preventing aflatoxin contamination based on three major axes: improving fungal resistance in crops, avoiding fungal contamination and reducing the toxigenic fungal population. Crop rotation, tillage, timely planting of resistant seed varieties, weed control, preventive management of insect infestations and irrigation are just some of the ways of preventing aflatoxin production [9]. In fact, Kawashima *et al.* [31] showed that agricultural practices, in particular the crushing of maize grains, favoured fungal contamination and aflatoxin production because of the physical damage suffered by these grains during harvesting, as well as their immaturity. The correct application of these measures allows good control of fungal and aflatoxin risks [32]. However, it is important to stress that certain practices, although governed by laws in some countries, still do not guarantee food safety. In this regard, Brabet *et al.* [33] showed that the practices used in Brazil to prevent the production of aflatoxins in nuts unfortunately contributed to this. It is therefore important for countries to comply with CODEX standards.

Other techniques aimed at controlling water activity (a_w) to limit aflatoxin synthesis abound in the literature. Low water activity inhibits aflatoxin synthesis in cereals [34]. Lahouar [35] showed that a water activity (a_w) of less than 0.9 inhibits AFB1 synthesis in sorghum. As for hand sorting, it reduces aflatoxin levels in peanuts exposed to fungal contamination by more than 96% [35]. However, the best way to prevent the risks associated with fungal contamination remains awareness [36]. James *et al.* [36] have indeed shown a reduction in aflatoxin contamination of maize grains in West Africa following awareness sessions. The ignorance of the dangers related to aflatoxins by the main actors of the agricultural world contributes to the high contamination of foodstuffs by aflatoxins [37]. As for Negash [11], he proposes eight (8) preventive methods against the presence of aflatoxins in food and feed. There are purchase feed from reputable person and companies experienced in aflatoxin prevention, avoid to buy poor quality feed or feed ingredients, store feed at proper moisture levels, develop a systematic inspection and clean-up program to keep bins, delivery trucks and other equipment free of adhering or caked feed ingredients, minimize dust accumulation in milling and mixing areas, check feed storage bins for leaks, implement effective rodent and insect control programs in grain storage areas and treat contaminated grains with aflatoxins with ammonia. So, the persistent presence of aflatoxins despite compliance with preventive methods directs research towards other more radical means of combating the production of aflatoxins.

ajfand AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

Chemical control

It is based on the use of synthetic chemicals for various purposes, either to control fungal growth (fungistatic) or to eliminate it (fungicidal). In either case, the desired effect is dose-dependent. In 2022, work by Lehmane [38] showed that people in Benin used several techniques to protect maize stocks from fungal attack. Indeed, maize crops are among those most prone to aflatoxin contamination [9]. This work, therefore, reports widespread use of sofagrain, pyrimiphos-methyl, thiamethoxam, permethrin, deltamethrin and fumigant by the people of Benin to protect their maize in storage. The use of some of these chemicals, such as sofagrain, pyrimiphos-methyl and deltamethrin, as well as other non-recommended pesticides, had been reported since 2001 in the fight against aflatoxins in maize and yam pods by the people of Benin. Other chemicals such as arsenious anhydride and zinc phosphide are also used in Benin to preserve maize [38].

The negative impact of the use of these molecules and chemicals on human health, the environment and biodiversity open the door to exploring other prospects for antifungal and antiaflatoxin control [38].

Biological control

Gardener and Pal [39] define biological control as the deliberate use of introduced or resident living organisms, other than disease-resistant host plants, to suppress the activities and/or populations of pests, other than disease-resistant host plants, to suppress the activities and/or populations of one or more plant. It is, therefore, a non-chemical control method that involves using the natural predators to which pests are naturally susceptible to control their proliferation and nuisance. For example, it aims to degrade aflatoxin into non-toxic substances or adsorb aflatoxin using the secondary metabolites of microorganisms [32]. There are several biological control methods. Allelic recombination toxic and atoxic strains using isolates of non-toxic *A. flavus* strains combined with good cultural practices has been proposed by Moral *et al.* [12] as a biological control method. Jallow *et al.* [27] report more elaborate methods involving bacterial control by microbial competition of biocontrol of fungal growth and aflatoxin biosynthesis as well as fungal control based on the use of certain fungal species to block synthesis of aflatoxins or simply degrade aflatoxins when it is produced. Furthermore, Loi *et al.* [28] demonstrated that control of fungal growth as well as aflatoxins biosynthesis can be achieved through the use of natural substances such as antioxidants gallic acid and caffeic acid, phenolics compounds, caffeic acid and gallic acid, hydrolysable tannins (gallic acid), flavonoids and lignans, and nitrogenous compounds such as glucosinolates and alkaloids extracted from plants. These substances have the greatest antifungal and aflatoxin biosynthesis inhibitory activity [28].

https://doi.org/10.18697/ajfand.128.24315

ajfand AFRICAN JOURNAL OF FOOD, AGRICULTURE, NUTRITION AND DEVELOPMENT
SCHOLARLY, PEER REVIEWED
Volume 24 No. 3
March 2024
PUBLISHED BY AFRICAN SCHOLARLY SCIENCE COMMUNICATIONS TRUST
ISSN 1684 5374

Other natural antioxidant substances such as caffeic acid have inhibitory effects on aflatoxin synthesis. More recently, studies by Hernandez *et al.* [40] revealed that phenolic compounds such as condensed tannins have strong antioxidant and antiaflatoxin B1 activities on *Aspergillus flavus* species. Piperine inhibits aflatoxin production and fungal growth by interfering with the action of regulatory genes. Jallow *et al.* [27] reported that carvacrol, cinnamaldehyde, eugenol, limonene, terpineol, thymol and turmerone found in plant extracts were bioactive in inhibiting fungal growth and aflatoxin biosynthesis. Their mode of action is simple; Loi *et al.* [28] has shown that bioactive compounds extracted from plants alter the vital functions of the fungi, such as weakening ergosterol metabolism, inducing intracellular changes, inhibiting cytoplasmic and mitochondrial proteins, modifying osmotic pressure and irreversible membrane alterations. However, the fungal growth inhibitory activity of these plant bioactive compounds is not generally correlated with that of aflatoxin inhibition [40]. Certain compounds can specifically block fungal growth without having any effect on aflatoxin production and vice versa. In addition to the aqueous and organic plant extracts and isolated molecules mentioned above, essential oils have dose-dependent fungicidal, fungistatic and antiaflatoxinogenic activities [40].

Plants of interest

The controversy surrounding the use of phytosanitary products and by-products has opened up new avenues for combating fungi and their toxins. It is now possible to control the proliferation of fungal contaminants and their secondary metabolites by using the properties of certain plants. To this end, they have shown that the aqueous extract of *Mimosa tenuiflora* had a significant impact on the antiaflatoxin B1 activity of *Aspergillus flavus* [40]. Lehmane also reports the use of ash and plant species such as neem (*Azadirachta indica*) by people in Benin to preserve maize seeds during storage [38]. In 2019, Adjovi *et al.* [20] demonstrated the antifungal and antiaflatoxic activity of *Laurus nobilis* essential oil on *A. flavus*. Also, *A. flavus* was unable to carry out aflatoxin biosynthesis on cassava despite significant fungal development [19]. These highly encouraging results pave the way for the exploration of plant flora.

CONCLUSION, AND RECOMMENDATIONS FOR DEVELOPMENT

The proliferation of fungal contaminants in foodstuffs is a real danger and a serious public health problem for countries around the world. Faced with the many dangers posed by aflatoxins, particularly aflatoxin B1, various control techniques have been developed. Although preventive control is the most widely recommended method, it remains a luxury for many people because it is very restrictive and does not always guarantee the safety of foodstuffs. Chemical control, although effective, also has its shortcomings, with impacts on biodiversity and the environment, as well as the resulting fungal resistance. Biological control, which is more respectful of the environment, improves antifungal and antiaflatoxic control. But it is still insufficient, and above all it is reserved for a handful of people because of the manipulation of micro-organisms and the ethical problems involved. Using natural substances extracted from plants offers a better way of protecting foodstuffs against fungal proliferation and aflatoxin biosynthesis, with very satisfactory results. They are neither toxic to humans or animals, nor polluting, and naturally contain the secondary metabolites required to modulate fungal growth and reduce or even inhibit aflatoxin biosynthesis.

ACKNOWLEDGEMENTS

This work is the fruit of a personal investment and the contribution of the whole team of the Biochemistry and Molecular Biology Laboratory. A warm thank you to Dr (MC) Ingrid S. M. ADJOVI for training in documentary research and bibliometrics.

Impactful actions

For several years, we have created the multidisciplinary consortium "SCIENCE & ME" which brings together teacher-researchers of different CAMES grades from public universities in Benin, namely the University of Abomey-Calavi (UAC), the National University of Agriculture (UNA) and University of Parakou (UP). This consortium implemented the concept of *“Science for All”* whose main objective is to bring science closer to grassroots populations in order to popularize the research results of the laboratories and research institutes of the said universities. It works with municipal, communal and local elected officials in the various communes of Benin through communication, awareness and information panels in local languages. The 1st edition of *"Science Pour Tous"* whose theme is *"Diversity of scientific views on the development of local resources"* was held in the commune of Lokossa, on May 19, 2023, under the patronage of the Mayor assisted by its local councilors and elected officials.

We believe we can use this sector (Science Pour Tous) to advance the policy in terms of agricultural production management in order to guarantee the health safety of foodstuffs offered to populations at the municipal and local level during our next editions of *"Science Pour Tous"*. We also intend to take advantage of the International Food Safety Day (JISSA) which is held every June 7 through a general public conference within the Faculty of Sciences and Health of the University of Abomey-Calavi.

The attached files are some proof of actions aimed at promoting and popularizing the results of our research.

https://doi.org/10.18697/ajfand.128.24315

Conflict of Interest

The authors declare that the research was conducted in absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions

No external authors contributed to this study.

Funding

There is any financial aid from any sponsors.

REFERENCES

1. **Diom M** Etude des problèmes posés par les aflatoxines dans les aliments du bétail et de l'homme. 1978; Thèse n° 12 École Inter-États des Sciences et Médecine Vétérinaires. P.38.

2. **Hintermann J and B Ninard** Les tumeurs de la travée hépatique chez le porc au Maroc. *Bull. Inst. Hyg. du Maroc.* 1945; **5:** 49 - 57.

3. **International Agency for Research on Cancer (IARC).** Monograph on Evaluation of Carcinogenic Risk to Humans, World Health Organization. Some traditional Herbal Medicines, some Mycotoxins, Naphthalene and styrene. *Summary of Data Report and Evaluation.* 2002; **vol 82.** Lyon, pp. 171-175.

4. **Food and Agriculture Organization (FAO).** Worldwide regulations for mycotoxins in food and feed in 2003, Rome, Italy. 2004 http://www.fao.org/3/y5499e/y5499e00.htm

5. **World Health Organisation (WHO).** The aflatoxins. 2018; 1–6.

6. **Popiel D, Dawidziuk A, Koczyk G, Mackowiak A and K Marcinkowska** Multiple facets of response to fungicides – the influence of azole treatment on expression of key mycotoxin biosynthetic genes and candidate resistance factors in the control of resistant Fusarium strains. *European Journal of Plant Pathology*. 2017; **147(4):** 773-785. https://doi.org/10.1007/s10658-016-1042-3

7. **Ehrlich KC and J Yu** Aflatoxin biosynthetic pathway and pathway genes (pp. 41-66). London, 2011; UK: INTECH Open Access Publisher.

8. **Ansari MS, Moraiet MA and S Ahmad** Insecticides: impact on the environment and human health. *Environmental deterioration and human health: natural and anthropogenic determinants*. 2014; **99:** 123.

9. **Partnership for Aflatoxin Control in Africa (PACA).** Lutte contre l'aflatoxine pour l'accroissement des échanges commerciaux, une meilleure santé et des économies dynamiques en Afrique. © Burleigh Dodds Science Publishing Limited, 2017. All rights reserved. http://dx.doi.org/10.19103/AS.2016.0002.23

10. **Bailly S, El Mahgubi A, Carvajal-Campos A, Lorber S, Puel O, Oswald IP, Bailly J-D and B Orlando** Occurrence and Identification of *Aspergillus* Section *Flavi* in the Context of the Emergence of Aflatoxins in French Maize. Toxins 2018; 10(12). https://doi.org/10.3390/toxins10120525

11. **Negash D** A Review of Aflatoxin: occurrence, Prevention, and Gaps in Both Food and Feed Safety. *J Appl Microb Res*. 2018; **Vol: 1 Issue: 1** (35-43).

12. **Moral J, Garcia-Lopez MT, Gordon A, Ortega-Beltran A, Puckett R, Tomari K, Gradziel T M and TJ Michailides** Resistance to *Aspergillus flavus* and *Aspergillus parasiticus* in Almond Advanced Selections and Cultivars and Its Interaction with the Aflatoxin Biocontrol Strategy. *Plant Dis.* 2022;**106(2):** 504-509. https://doi.org/10.1094/PDIS-05-21-0892-RE Epub 2022 Feb 5. PMID: 34569835.

13. **Verheecke C, Liboz T, Darriet M, Sabaou N and F Mathieu** *In vitro* interaction of actinomycetes isolates with *Aspergillus flavus*: impact on aflatoxins B1 and B2 production. *Letters in Applied Microbiology.* 2014; **58:** 597–603.

14. **Aberedew K and A Ayelign** Aflatoxin contamination in red pepper from producers in Addis Ababa. *Food Addit Contam Part B Surveill*. 2022; **16 (1):**1-7. https://doi.org/10.1080/19393210.2022.2102678 Epub 2022 Jul 19. PMID: 35854632.

15. **Giorni P, Magan N, Pietri A and P Battilani** Growth and aflatoxin production of an Italian strain of *Aspergillus flavus*: influence of ecological factors and nutritional substrates. *World Mycotoxin Journal.* 2011; **4:** 425–432.

16. **Aldred D and N Magan** Post-harvest control strategies: Minimizing mycotoxins in the food chain. *International Journal of Food Microbiology, Mycotoxins from the Field to the Table.* 2007; **119:** 131–139.

17. **Sharma RP** Mycotoxins in the food chain: a look at their impact on immunological responses. In Nutritional biotechnology in the feed and food industries. Proceedings of Alltech's 20th Annual Symposium: re-imagining the feed industry, Lexington, Kentucky, USA, 23-26 May. 2004; (pp. 305-314). Alltech UK.

18. **Gnonlonfin G, Adjovi YCS, Tokpo A, Agbekponou E, Ameyapoh Y, de Souza C, Brimer L and A Sanni** Mycobiota and identification of aflatoxin gene cluster in marketed spices in West Africa. *Food Control.* 2013; **34(1):** 115-120.

19. **Adjovi YCS, Bailly S, Gnonlonfin BJG, Tadrist S, Querin A, Sanni A, Oswald IP, Puel O and J-D Bailly** Analysis of the contrast between natural occurrence of toxigenic Aspergillii of the *Flavi* section and aflatoxin B1 in cassava. *J. Food Microbiol.,* 2013; **Vol. 38:** 151–159.

20. **Adjovi YCS, Koulony R, Atindehou MC, Ahehehinnou UH, Dadavodou J and A Sanni** Laurus nobilis l. a natural alternative against *Aspergillus flavus* and aflatoxins. *International Journal of Development Research.* 2019; **09 (05):** 27692-27697.

21. **Marin S, Ramos AJ, Cano-Sancho G and V Sanchis** Mycotoxins: Occurrence, toxicology, and exposure assessment. *Food and Chemical Toxicology.* 2013; **60:** 218–237.

22. **Ostry V, Malir F, Toman J and Y Grosse** Mycotoxins as human carcinogens-The IARC Monographs classification. *Mycotoxin Research.* 2017; **33(1):** 65-73. http://dx.doi.org/10.1007/s12550-016-0265-7

23. **Martínez J, Hernández-Rodríguez M, Méndez-Albores A, Téllez-Isaías G, Mera Jiménez E, Nicolás-Vázquez MI and RM Ruvalcaba** Computational Studies of Aflatoxin B_1 (AFB_1): A Review. *Toxins*. 2023; **15(2):** 135. https://doi.org/10.3390/toxins15020135

24. **Täubel M, Sulyok M, Vishwanath V, Bloom E, Turunen M, Järvi K, Kauhanen E, Krska R, Hyvärinen A, Larsson L and A Nevalainen** Co-occurrence of toxic bacterial and fungal secondary metabolites in moisture-damaged indoor environments. *Indoor Air.* 2011; **21:** 368–375.

25. **Rustom IY** Aflatoxin in food and feed: occurrence, legislation and inactivation by physical methods. *Food Chemistry.* (1997); **59(1):** 57-67. https://doi.org/10.1016/s0308-8146(96)00096-9

26. **Khoury El R, Caceres I, Puel O, Bailly S, Atoui A, Oswald I, El Khoury A and J-D Bailly** Identification of the Anti-Aflatoxinogenic Activity of Micromeria graeca and Elucidation of Its Molecular Mechanism in *Aspergillus flavus*. *Toxins.* 2017; **9:** 87 https://doi.org/10.3390/toxins9030087

27. **Jallow A, Xie H, Tang X, Qi Z and P Li** Worldwide aflatoxin contamination of agricultural products and foods: From occurrence to control. *Comprehensive Reviews in Food Science and Food Safety.* 2021; **20:** 2332-2381.

28. **Loi M, Paciolla C, Logrieco AF and G Mulè** Plant Bioactive Compounds in Preand Postharvest Management for Aflatoxins Reduction. *Frontiers in Microbiology.* 2020; **11:** 243. https://doi.org/10.3389/fmicb.2020.00243

29. **Centre de coopération Internationale en Recherche Agronomique pour le Développement.** Inventaire des recherches conduites au Bénin portant sur l'impact des pratiques agricoles sur la santé humaine. Rapport de mission au Bénin 25 septembre au 6 octobre 2010.

30. **Azam K, Akhtar S, Gong Y, Routledge M, Ismail A, Oliveira C, Iqbal S and H Ali** Evaluation of the impact of activated filtration system on the concentration of aflatoxins and selected heavy metals in roasted coffee. **Food Control.** 2020; **121:**107583.

31. **Kawashima K, Siriacha P and S Kawasugi** Prevention of Aflatoxin Contamination in Thai Maize. *TARC Report JARQ.* 1993; **27:** 55-60.

32. **Chun HS and F Tian** Natural products for preventing and controlling aflatoxin contamination of food. Aflatoxin-Control, Analysis, Detection and Health Risks; Abdulra'uf, L., 2017; Ed, 13-44.

33. **Brabet C, Azevedo V, Alves dos Santos E, Quaresma M, Medeiros L, Nogueira M, Leite de Souza M, de Souza V, Lindblad M and M Olsen** Technical recommendations for the prevention and control of aflatoxins in the Brasil nut production chain. In Worldwide mycotoxin reduction in food and feed cahins. International Society for Mycotoxicology. 2009.

34. **Lahouar A, Marin S, Crespo-Sempere A, Saïd S and V Sanchis** Effects of temperature, water activity and incubation time on fungal growth and aflatoxin B1 production by toxinogenic *Aspergillus flavus* isolates on sorghum seeds. *Revista Argentina de microbiologia,* 2016; **48(1):** 78-85.

35. **Xu Y, Doel A, Wastson S, Routledge M, Elliott CT, Moore SE and YY Gong** Study of an educational hand sorting intervention for reducing aflatoxin B1 in groundnuts in rural Gambia. *Journal of Food Protection.* 2017; **80(1):** 44-49. https://doi.org/10.4315/0362-028x.JFP-16-3097

36. **James B, Adda C and K Cardwell** Public information campaign on aflatoxin contamination of maize grains in market stores in Benin, Ghana and Togo. *Food Additives and Contaminants.* 2007; **24(11):** 1283-1291.

37. **Anitha S, Tsusaka T, Njoroge S, Kumwenda N, Kachulu L, Maruwo J, Masumba J, Tavares A, Heinrich G, Siambi M and P Okori** Knowledge, attitude and pratice of Malawian farmers on pre-and post-harvest crop management to mitigate aflatoxin contamination in groundnut, maize and sorghum-Implication for behavioral change. *Toxins*. 2019; **11(12):** 716. https://doi.org/10.3390/toxins11120716

38. **Lehmane H, Ba R, Dah-Nouvlessounon D, Sina H, Roko G, Bade FT, Socohou A, Adjanohoun A and L Baba-Moussa** Status of Techniques Used to Control Moulds in Maize Storage in Africa. *Agricultural Sciences.* 2022; **13:** 49-64. https://doi.org/10.4236/as.2022.131005

39. **Gardener BM and KK Pal** Biological Control of Plant Pathogens. *The Plant Health Instructor*. 2006. https://doi.org/10.1094/PHI-A-2006-1117-02

40. **Hernandez C, Cadenillas L, Mathieu C, Bailly J-D and V Durrieu** Preservation of Mimosa tenuiflora Antiaflatoxigenic Activity Using Microencapsulation by Spray-Drying. *Molecules.* 2022; **27:** 496. https://doi.org/10.3390/molecules27020496