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Sustainable Control Strategies for Mycotoxigenic Fungi and Their Metabolites in Food Safety: Review

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Abstract

Mycotoxins, toxic secondary metabolites, contaminate 60-80% of agricultural crops. Their consumption through diet can affect human and animal health, causing cancer, teratogenesis, mutagenesis and immunosuppression. It is a relevant issue worldwide, because it represents a challenge that puts food safety at risk. The aim of this work was to review the main strategies for the sustainable control of mycotoxigenic fungi and their metabolites in food safety. Systematic research and a bibliographic analysis were performed using the following databases: SCOPUS, Science Direct, Web of Science and MDPI. Scientific articles, review articles and pages of organizations with worldwide intervention were consulted. The inclusion criteria included the keywords: mycotoxigenic fungi, mycotoxins, agriculture, biocontrol, and health. They also included bibliographic citations mainly from 2012 to 2022, although there are citations prior to this year that are relevant. This review summarizes alternatives found in research works, such as: immunoassays, biosensors, membranes, matrices, biological treatments, ozone, and UV radiation, among others. In conclusion, detection methods must be fast, inexpensive, sensitive, and selective, which guarantee food safety.

Keywords: Mycotoxins; Fungi; Agricultural crops; Control Strategies; Food Safety

Abbreviations: FAO: Food and Agriculture Organization; ITS: Internal Transcribed Spacer Regions; SERS: Surface Enhanced Raman Scattering; LOD: Limit of Detection

Introduction

Extreme events caused by climate change, economic or geopolitical shocks, and pest or disease epidemics can induce, spread, and prolong food insecurity. These direct and indirect effects lead to reductions in the availability of, and access to, healthy and nutritious food [1,2]. The magnitude, extent, and complexity of the threats posed by extreme events to global food security can further create cascading and systemic impacts that are difficult to predict or plan and prepare for [3,4]. The volume and quality of crops is mainly affected by pests, diseases, factors such as temperature, soil salinity, soil nutrient deficiency, and drought [5]. So too, the increase in the proliferation of mycotoxigenic fungi and their metabolites can have serious side effects on agri-food crops. According to the FAO (Food and Agriculture Organization of the United Nations) around 25% of food crops worldwide are affected by mycotoxigenic fungi, generating food losses of 1 billion tons per year [6]. Global climate change is expected to cause some species

of mycotoxigenic fungi to dominate others, increasing mycotoxin production [7]. The consumption of these metabolites through diet generates a wide range of disorders, from gastroenteritis to cancer in humans and animals, which is why it is considered a public health problem in the world [8]. Due to this, there is a growing interest in new legislation that restricts the trade of chemical pesticides. The above encourages the development of new fungal pesticides that are friendly to the environment and do not generate toxic residues [9]. Because sustainable measures are necessary to control mycotoxigenic fungi and their metabolites. The aim of these paper was to review the main sustainable control strategies for mycotoxigenic fungi and their metabolites in food safety. To fully achieve this purpose, the following topics are addressed:

i. We describe the relationship between global warming and the development of mycotoxigenic fungi in crops.

ii. We present and discuss the main mycotoxins.

iii. We explain some novel control strategies to prevent fungal development and toxin production in food safety.

Mycotoxigenic fungi in crops, global warming

The agricultural system and a wide variety of foods for human and animal consumption are susceptible to contamination by mycotoxigenic fungi of the *Aspergillus, Penicillium* and *Fusarium* genera, which can cause severe damage to farmers and ranchers (Table 1) [10]. Although fungi can colonize cereals before or after harvest, colonization and proliferation depend on environmental and ecological conditions, because the resulting mycotoxin production will be different (Figure 1) [11]. Climate change has influenced the increase in temperature, as well as the variation in rainfall, modifying the scarcity of species even in cold regions [12]. For example, the current level of CO_2 has increased from 280 to 400 ppm, which has contributed to the effects of global warming [11]. Farming communities have the appropriate knowledge of the environment in which they farm, to obtain the best yields. However, if the weather changes, agricultural practices must be adjusted to maintain productivity [13]. Due to, changing adaptive associations under global climate change will modify the outcome of microbial plant-soil interactions. Which will affect crop production, food, and feed supply and quality, like so negatively affecting plant physiology [14]. It has been reported that, with high or low temperatures, the growth of fungi and the production of their metabolites is inevitable. Atanda et al., observed that temperatures below 20 °C favored *Penicillium*, while temperatures above 20 °C increased the growth of *Aspergillus* species. They also report that legumes and cereals are the food products most likely to be contaminated by Aspergillus species, even during storage because there is no temperature control [15].

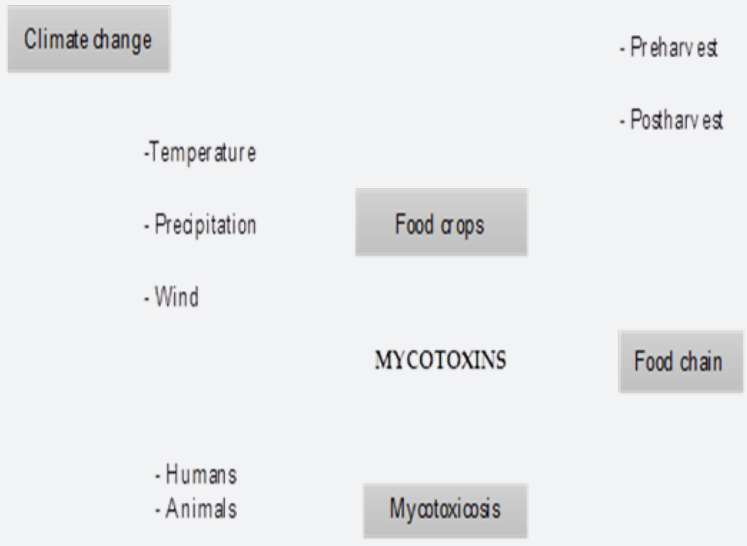

Figure 1: Influence of climate change on mycotoxin production.

Aspergillus, Fusarium and *Penicillium*

Aspergillus flavus is one of the most frequently isolated species in agriculture and medicine, it is cosmopolitan and contaminates a wide range of crops in the world [23]. Aflatoxin contamination causes significant annual crop losses internationally. Contaminating food products include cereals, pistachios, tree nuts and peanuts, spices, and figs in hot climates, aflatoxin production occurs anywhere in the food supply chain, from preharvest to consumer (Wei et al., 2019; Zhang et al., 2022b). Most grain storage structures used by farmers do not provide the proper internal atmosphere, they do not give maximum protection against water, insects, and rodents; and they are not easy to clean. All these

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conditions promote fungal growth and aflatoxin production in stored grains and legumes [25]. Toxinogenic strains of *Aspergillus flavus* tend to produce higher levels of aflatoxin B1 (AFB1) and aflatoxin B2 (AFB2), while A. parasiticus produces more equal amounts of AFB1, AFB2, aflatoxin G1 (AFG1), and aflatoxin G2 (AFG2) [26]. The phenotypic identification of this species is generally based on microscopic and macroscopic criteria, which consider the characteristics of conidiophores, phialides and spores, and colonial characteristics [27].

Table 1: Mycotoxigenic species and contaminating foods.

Mycotoxins	Fungal species	Contaminated food	References
Aflatoxins	*Aspergillus flavus, A. parasiticus*	Peanuts, wheat, corn, white cheese, tree nuts, milk, figs, eggs	[16]
Fumonisins	*Fusarium verticillioides, F. proliferatum*	Corn, milk, meat, legumes, potatoes	[17, 18]
Ochratoxin A (OTA)	*Aspergillus ochraceus, A. carbonarius, Penicillium verrucosum*	Cereals, legumes, nuts, cheese, pork, coffee, raisins, grapes, nuts, wine	[19]
Toxin T-2	*Fusarium sporotrichioides*	Corn, wheat, barley, oats, rye	[20]
Deoxynivalenol (DON)	*Fusarium graminearum*	Wheat, corn, rye, oats	[21]
Zearalenone (ZEN)	*F. culmorum, F. graminearum, F. crookwellense*	Corn, wheat, barley, oats, rice, sorghum, soybeans	[16]
Patulin (PAT)	*Penicillium expansum*	Apple, apple-based products, vegetables	[22]

However, micro and macromorphological characteristics are not sufficient for correct identification in atypical *Aspergillus* isolates, which include those strains that present slow sporulation, or in the presence of cryptic or sister *Aspergillus* species. Furthermore, carrying out identification through these methods alone is time-consuming and requires considerable technical knowledge [28]. For this reason, there is a growing interest in polyphasic identification that includes not only phenotypic identification, but also genotypic identification, through molecular techniques. These molecular techniques are based on the partial or total sequencing of the genome of different genetic targets, including the internal transcribed spacer regions (ITS) of rDNA and genes that code for proteins such as calmodulin and β-tubulin (Nasri et al., 2015). Although *Aspergillus fumigatus* is the main causal agent of aspergillosis in humans and other animals, *Aspergillus flavus* is also of importance in this condition, which includes allergic, saprophytic colonizing and invasive aspergillosis [30]. The importance of this species is that it is the second main pathogen causing invasive and non-invasive aspergillosis [31]. Furthermore, *A. flavus* has been identified as one of the main causes of fungal keratitis, a fungal infection of the cornea [32]. Therefore, the correct identification of the species *Aspergillus* genus is important because these are the causal agent of a wide spectrum of clinical presentations, within these manifestations is bronchopulmonary aspergillosis, otomycosis, skin conditions, colonization of cavities and invasive aspergillosis (Nasri et al., 2015).

Fusarium is considered opportunistic due to its ability to grow at 37 °C. Some of its species are producers of toxins which can affect man and animals. About 100 species have been described, of which 12 are considered pathogenic for man, among these are *F. solani, F. oxysporum* and *F. verticilloides*. It is a genus of great economic importance because they act as phytopathogens [34,35]. The genus *Penicillium* is a cosmopolitan genus that can grow on various substrates such as grains, fruits, nuts; it is one of the main contaminants in the postharvest phase [36]. It is important in animal and human nutrition due to the deterioration it produces in grains, in addition to producing toxins [37]. Many of the species belonging to *Penicillium* are abundant in the soil, as they can compete for organic substrates. In addition to this, its proliferation in food is easy, representing a serious problem for their conservation, in addition to being a potentially mycotoxigenic fungus, some of its species are producers of the mycotoxin called ochratoxin present in various foods, and which is considered nephrotoxic, inmunotoxic, teratogenic, in addition, the IARC (International Agency for Research on Cancer) classifies it within class 2B for being a probable human carcinogen [38]. Some other *Penicillium* species are important fruit pathogens during the postharvest period, and others are beneficial and widely used in the pharmaceutical and food industries [5].

Mycotoxins

The first reported signs of mycotoxicosis due to the consumption of food contaminated by mycotoxins arose in the Middle Ages in Europe. There are around 400 mycotoxins with toxigenic potential, produced by around 100 fungi [39,40]. Mycotoxins are naturally generated by certain filamentous fungal species, are chemically stable and heat resistant, so they can persist during food processing (OMS 2018). Two routes of exposure to these metabolites have been identified, through inhalation (frequently spores) and through diet, which can generate health effects for both humans and livestock [41,42]. The main effects are inmunotoxic, teratogenic, nephrotoxic, and carcinogenic. The most studied mycotoxins due to their effects on human and animal health, in addition to being important from the agroeconomic point of view, commonly found in food

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are aflatoxins, zearalenone, fumonisins, trichothecenes, and ochratoxin A [43]. Mycotoxin contamination in the food chain is mainly conditioned by the diversity of fungal strains, the fungal vulnerability of the plant in the field, the microbial population, humidity, temperature, nutrients, and stress factors [44]. Fungal activity and toxin production elsewhere have been reported to be optimal at 25-37 °C [45]. In a study conducted by Zhao et al., they reported that 81.5% of feed ingredients were contaminated by aflatoxin B1, deoxynivalenol and zearalenone, while 95.7% of complete feeds were contaminated by these mycotoxins in various combinations [46]. In another study conducted by Ma et al they reported contamination by different mycotoxins in foods from different provinces of China with the following levels of contamination: AFB1 83.3%, ZEN 88.0% and DON 74.5% [47].

Aflatoxins

Aflatoxins consist of a group of approximately 20 related fungal metabolites, although the most studied for contaminating food are AFB1, AFB2, AFG1 and AFG2. *Aspergillus flavus* and *A. parasiticus* species are the main producers of aflatoxins and can grow on a wide variety of substrates. Their ability to produce aflatoxins depends on their individual metabolic system, essential for primary lipid metabolism, and specific enzymes (synthetases) capable of producing this secondary metabolite [48]. It should be noted that the synthesis of aflatoxins is not characteristic of the species, but of the strain [5]. These toxic substances are of low molecular weight, odorless, tasteless, and colorless, stable in food, it is also resistant, as it is not easily degraded by cooking processes [49-51]. High temperatures and humidity favor the growth of mycotoxin-producing fungi, so countries with these environmental conditions often experience increased contamination (Rushing and Selim, 2019). In addition to this, climate change has been modifying the variation in precipitation and temperature, this has meant that there are more regions prone to AFB1 contamination problems. Even that this contamination increases in crops where there were already problems due to this metabolite (Bbosa, G. S., Kitya, D., Lubega, A., Ogwal-Okeng, J., Anokbonggo, W. W., & Kyegombe, 2013, Rushing and Selim, 2019). Water content is a key determinant of aflatoxin development in food crops. To produce toxins by *A. flavus*, approximately 13% relative humidity and a water activity (a_w) of 0.65 are required [15], however 0.77 of a_w or more is optimal for growth and proliferation [54]. Aflatoxins are classified according to their chemical structure in the difurocomarocyclopentenone and difurocoumarolactone series, Table 2 shows the types of aflatoxins and their generalities.

Table 2: Aflatoxin's classification of and its main toxic characteristics.

Serie	Aflatoxins	Generalities	References
DC	Aflatoxin B_1	Potent hepatotoxic and hepatocarcinogenic mycotoxin.	[59]
	Aflatoxin B_2	Development of cancer, from which aflatoxin M2 is formed.	[60]
	Aflatoxin B_{2a}	Aflatoxin B2a (hydroxydihydro-aflatoxin B1) has lower toxicity and DNA binding than AFB1.	[61]
	Aflatoxin M_1	It is a hydroxylated metabolite of AFB1, it is resistant to thermal inactivation, pasteurization, auto-claving.	[62]
	Aflatoxin M_2	It is a hydroxylated metabolite of AFB2.	[63]
	Aflatoxicol	It is a metabolite of AFB1, but less mutagenic.	[64]
DL	Aflatoxin G_1	Causes a chronic pulmonary inflammatory response, which is associated with oxidative damage to alveolar epithelial cells.	[65]
	Aflatoxin G_2	Dihydroxy derivative of aflatoxin G1.	[49]
	Aflatoxin GM_1	Basic and extremely weak polycyclic aromatic compounds.	[66]
	Aflatoxin GM_2	Extremely weak basic compound (essentially neutral). Metabolite of Aflatoxin G2.	[49]

DF: Difuranocumarines; DC: Difurocoumarociclopentenone; DL: Difurocoumarolactone

Exposure to aflatoxins is of relevance in the health sector, in 2004 alone it was reported that approximately 4.5 billion people in developing countries were at risk of chronic and uncontrolled disease [15]. In a study carried out by Abdel et al. reported a maximum *Aspergillus* growth rate of 6.9 mm/day at 35 °C and a maximum aflatoxin production rate of 2278-3082 µg/g at 37 °C in maize [55]. Wajih ul Hassan et al. reported aflatoxin contamination in maize in Pakistan, in all the samples there was aflatoxin contamination with limits higher than 20 µg/kg, in addition there was a higher concentration of AFG1 in all the maize varieties analyzed [56]. Even though the globalized world has allowed countries to take advantage of the tools to reduce the levels of aflatoxins in food, it is evident that developed countries have less risk of eating food contaminated with these metabolites compared to developing countries, due to the policies and mismanagement of operations in agriculture (Waliyar et al., 2015). In a study conducted in regions of Ghana by Sugri et al. farmers were surveyed to assess their knowledge about aflatoxins, 78% of the respondents knew about aflatoxins, however, 68.1% did not perceive aflatoxins as a major food safety problem. In this same study, aflatoxin contamination in corn samples will be limited to a range of 0.011 to 308 mg/kg (Sugri et al., 2015).

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Ochratoxin A

Among the ochratoxins that have been described are: β, α, A, B and C, however, it is reported that the most toxic is OTA (Ochratoxin A). OTA is one of the most important mycotoxins worldwide because it generates on human and animal health, within the effects it generates are nephrotoxic, mutagenic, teratogenic and inmunotoxic: this metabolite is generated by both *Aspergillus* and *Penicillium* species [67]. According to the IARC, it is in group 2B as a possibly carcinogenic substance [68]. The target organ of ochratoxin A is the kidneys, which is why it is associated with nephropathies [69]. It contaminates a wide variety of foods, including cereals, fruits, vegetables, spices, and animal products [70]. OTA is a white, odorless, crystalline solid compound, when absorbing ultraviolet light, it exhibits a strong fluorescence, which depends largely on the pH, the solubility in water is approximately 0.42 mg/L at 25 °C and exhibits moderate solubility in polar organic solvents such as chloroform, ethanol, and methanol [71]. Because OTA compromises food safety, it is necessary to monitor this metabolite in food, its detection is mainly based on chromatography and immunoassays, but when using these methods there are limiting factors such as costs, processing time and trained personnel (Sugri et al., 2015; Waliyar et al., 2015). In a study by Wajih et al. contamination in corn by OTA in Pakistan was determined, reporting that 71% of the samples presented contamination by this metabolite in a range of 2.14 to 214 µg/kg [74]. Majeed et al. report contamination by ochratoxin A with a value of 5.29 µg/kg in corn samples [75]. In another study by Ibáñez et al. in cereal samples obtained from a Spanish market, ochratoxin A contamination was reported in 39% of the analyzed samples of wheat and rice, whose values were 0.37 µg/kg [76].

Fumonisins

The *Fusarium* genus is the most prevalent plant pathogen invading agricultural crops, and the mycotoxins produced by species of this genus are the most economically important [77]. Within the group of metabolites produced by this genus, the most important due to their toxicity in humans and animals are fumonisins (FB), zearalenone (ZEA) and trichothecenes [78]. There are about 15 fumonisins, but the most studied are fumonisins B1 (FB1), B2 (FB2) and B3 (FB3), of which the most toxic is FB1 and is classified within group 2B as a possibly carcinogenic substance in humans, by IARC [79, 80].

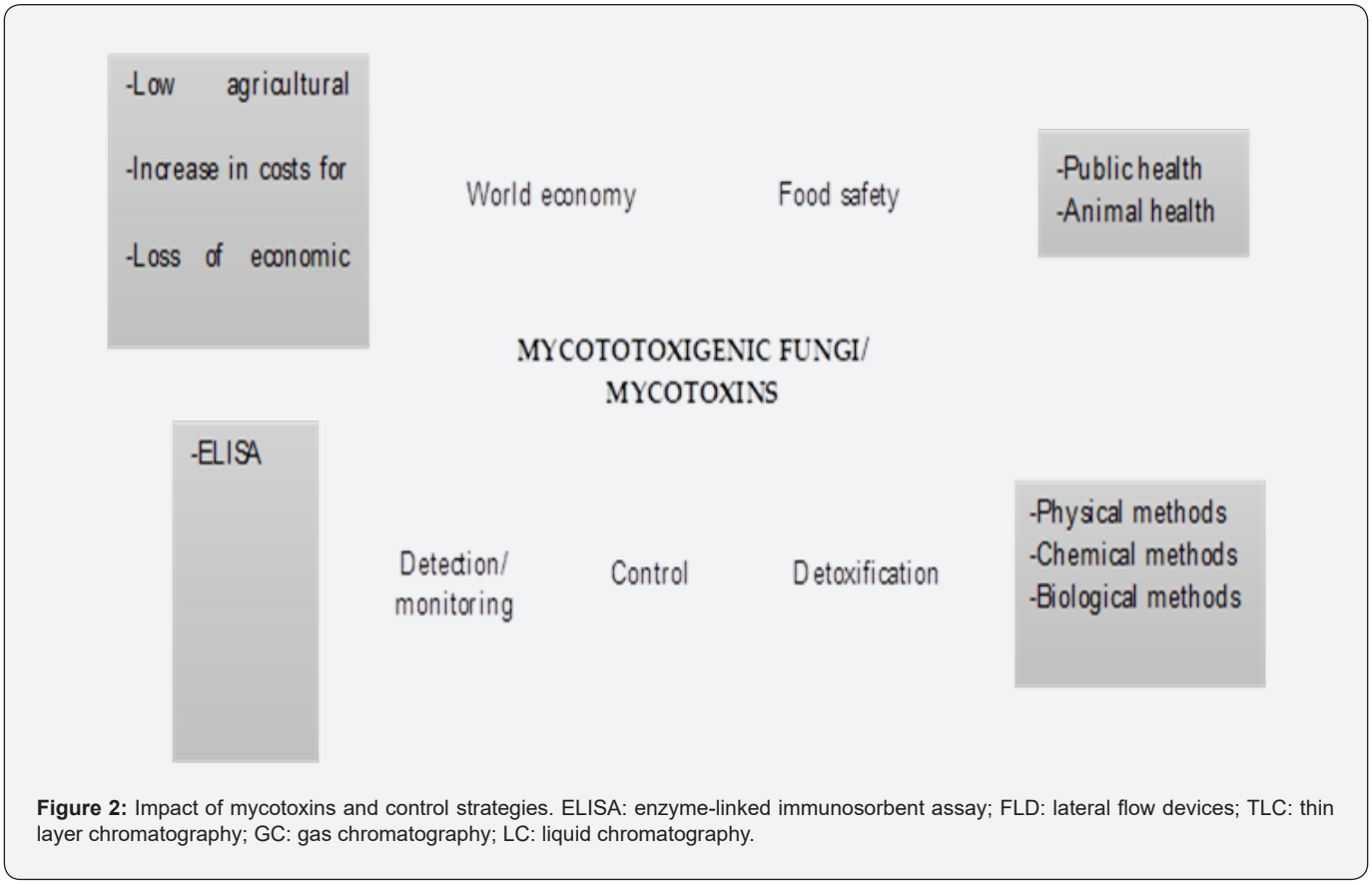

Figure 2: Impact of mycotoxins and control strategies. ELISA: enzyme-linked immunosorbent assay; FLD: lateral flow devices; TLC: thin layer chromatography; GC: gas chromatography; LC: liquid chromatography.

Control Strategies

Since mycotoxins can cause toxicity in animals and humans, there is a growing interest in the control or elimination of mycotoxigenic fungi and/or their metabolites. One of the systems affected by these metabolites is the agri-food system, which must guarantee the supply of sufficient and quality food. However, among the substances that compromise food safety are

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mycotoxins, which represent a danger to food safety and to global health [81]. There are two strategic approaches aimed at the control of these fungal secondary metabolites. The first consists of the prevention of mycotoxins, which implies the inhibition of fungal growth, and the second consists of detoxification whose objective is to eliminate the fungal metabolite. Figure 2 shows the negative impact of mycotoxins on the world economy and food security. The latter being able to affect human and animal health; as well as strategies aimed at the control of mycotoxigenic fungi and their metabolites.

Detection

There are multiple techniques for the detection of mycotoxins, however, in a study conducted by Wei et al. the efficacy of surface plasmon resonance (SPR) was determined as a rapid detection method for mycotoxins in corn and wheat, the results showed that the minimum detection limits of ochratoxin A, AFB1, deoxynivalenol, and zearalenone were 1.27 ng/ml, 0.59 ng/ml, 3.26 ng/ml, and 7.07 ng/ml, respectively [82]. Transducers have also been used, where the main detection method is the use of optical, piezoelectric, and electrochemical spectroscopy. In addition, biological materials such as peptides, enzymes, antibodies, cells, and nucleic acids are important elements in detection in biosensor studies [83]. Chen et al, described an *Escherichia coli*-based biosensor to evaluate AFB1 and ZEN (zearalenone) in peanut and corn oil samples. In this study they report the decrease in the concentration of AFB1 in the range of 0.01-0.3 µg/mL and of ZEN in a range of 0.05-0.5 µg/mL. They conclude that the method establishes a new approach for the detection of mycotoxins [84].

The damage caused by mycotoxins in human and animal health requires the development of effective detection methods. Immunoassays are a sensitive and highly specific tool for the rapid detection of mycotoxins [85]. Zhang et al. developed a multiple surface enhanced Raman scattering (SERS)-based lateral flow immunosensor to determine six major mycotoxins in maize. The results showed a recovery of 78.9 to 106.2% and a high precision of the assay, in addition to being an assay that is completed in less than 20 minutes [86]. Yan et al. used a mimotope of deoxynivalenol which specifically binds to anti-DON antibody. In this study, an average recovery in corn and wheat samples of 90.4% to 118% and 101.3% to 111%, respectively, was obtained [85]. In another study conducted by Yang et al. developed an active signal electrochemiluminescence (ECL) biosensor for OTA determination, the results showed that ECL has a linear relationship with OTA in the range of 0.05 to 500 pg/mL with a correlation coefficient of 0.9957, with the limit of detection (LOD) being 0.02 pg/mL [87]. Therefore, the use of this biosensor for the detection of OTA in corn samples can give satisfactory results. Other studies carried out for the detection of mycotoxins which have proven to be effective and in some cases being able to detect multiple mycotoxins, are described in Table 3. Due to the importance of these metabolites in the agri-food chain, it is necessary to develop new methods for detecting mycotoxins in food and feed, which are rapid, low cost, as well as sensitive and selective [88], because these metabolites compromise food safety by putting human and livestock health at risk.

Table 3: Mycotoxin detection methods.

Evaluated mycotoxins	Methods	Results	References
ZEN	Competitive upconversion-linked immunosorbent assay (ULISA)	Detection limit: 20 pg/mL^{-1} (63 pM).	[95]
AFB1, DON, FB1, toxin T-2, ZEN	Microarray lateral flow test strip using an organic luminescent compound	Detection limits were 1.3, 0.5, 0.4, 0.4, and 0.9 mg/kg, respectively	[96]
Toxin T2, ZEN, FB1	Biosensor with a mass-sensitive microarray	The sensitivity was 1.3, 2.0, and 6.8 ng/ml	[97]
ZEN	Modified polyvinyl chloride membranes.	Detected with a sensitivity of 14.1 ± 3 µA/µg	[98]
OTA, FB1, DON	SERS array based on reverse opal silica photonic crystal microspheres loaded with AuNP (gold nanoparticles)	Detection limits were 2.46 pg/mL, 0.20 pg/mL and 68.98 pg/mL	[99]
AFB1, OTA, ZEN	Quantum dot microsphere based immunochromatography test strip	Sensitively detects at low detection limits of 0.01, 0.2, and 0.032 ng/mL	[100]
AFB1	Fluorophore-based aptamer biosensor (Alexa Fluor 488) in combination with graphene oxide (GO)	Visible green bloom was observed at 20 mg/kg, which was interpreted as 20 mg/kg	[101]
AFB1	Surface enhanced Raman scattering radiometric aptasensor (SERS)	The detection limit was 0.6 pg/mL^{-1} in standard solution	[102]
ZEN, PAT	Fluorescent aptasensor based on graphene oxide and fluorescence resonance energy transfer (FRET)	The detection limit of this aptasensor was 2.29 nM for PAT and 0.037 nM	[103]
AFB1, OTA, ZEN	Catalytic Fork Assembly along with a Pregnancy Test Strip	Visual detection limits were 20.50 and 20 pg/mL, these can be obtained in 15 minutes	[104]

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Detoxification

It has been reported that the use of chemical fertilizers as the main fungal control measure is no longer efficient because chemical substances can destroy the ecological environment of the soil, resulting in fungal resistance [89]. Due to the above, there is a greater interest in the regulation of detoxification and detoxification of mycotoxins in food, from a physical, chemical, biological and nutritional approach [90]. The use of natural substances as an alternative in the detoxification of mycotoxigenic fungi and their metabolites is of great importance in food production. For example, the use of essential oils as a control measure is efficient due to its low toxicity, high volatility and because it is biodegradable [91]. The biosynthesis of mycotoxins is modulated by oxidative stress that occurs during the secondary exchange of fungi, through reactive oxygen species [44]. Therefore, there is a growing interest in the use of natural antioxidant substances that inhibit the growth of mycotoxigenic fungi and their metabolites, due to their non-toxicity and because they are friendly to the environment [92].

In a study carry out by Silva et al., the antifungal activity against *Aspergillus flavus* and *A. parasiticus* of the essential oils of fennel, ginger, peppermint and thyme was evaluated, reporting the following effective concentrations: 50, 80, 50 and 50% respectively [93]. Kalagatur et al. evaluated the antifungal activity on strains of *Aspergillus ochraceus* and *Penicillium verrucosum*, of the essential oils of *Cinnamomum zeylanicum* and *Cymbopogon martini*, demonstrating a complete fungal inhibition of growth and OTA production at 1500 and 2500 µg/g in corn grains, respectively [44]. Gemeda et al. evaluated the antifungal activity of the essential oils of *Cymbopogon martinii*, *Foeniculum vulgare* and *Trachyspermum ammi* against *Aspergillus* strains, the results showed a better efficacy of *T. ammi* oil, showing mycelial inhibition absolute at 1 µl/mL, in turn completely inhibited spore germination at a concentration of 2 µl/mL. Furthermore, it totally inhibited the production of aflatoxins from *A. niger* and *A. flavus* at 0.5 and 0.75 µl/mL, respectively [94].

In a study conducted by Gómez-Maldonado et al. the antifungal activity was evaluated from extracts of manila seeds, in the study they report an inhibition of mycelial growth against the fungus *Colletotrichum brevisporum* of 100% after 9 days and spore germination of 0% after 20 hours, with manila seed extract at 3 g/L [105]. Andleeb et al. carried out a study in which they report an antifungal activity greater than 50% on strains of *A. fumigatus* and *A. niger*, by using extracts from flowers, berries and leaves of *Argemone mexicana* L. [106]. Rodriguez et al. carried out a study in which they report an 85% inhibition on the germination of *F. oxysporum* conidia on the fifth day of treatment, using phenolic extracts obtained from chiltepin fruits [107]. *Trichoderma* is a fungus widely studied in the world for its antifungal capabilities, as well as for promoting plant growth [108]. *Trichoderma spp.* it is cosmopolitan, it is characterized by the fact that it grows rapidly, in addition to having a metabolic diversity, even many of its species interact with animals, plants and other fungi [109]. In a study by He et al., showed that *Trichoderma asperellum* decreases the accumulation of DON (deoxynivatenol) and FB1 in the stem and cob of maize grown in soil [89]. Saravanakumar et al. determined that the cellulase genes Thph1 and Thph2 of *Trichoderma harzianum*, in addition to controlling foliar disease in corn, also act as biocontrol in stem rot caused by *Fusarium* [84].

In another study by Li et al. evaluated the efficacy of *Sporidiobolus pararoseus* Y16 against grape rot caused by *Aspergillus niger*, showing that at different concentrations of *S. pararoseus* Y16 the decomposition of table grapes by *A. niger* was significantly inhibited [51]. For their part Kinyungu et al. evaluated biological control treatments from harvest to storage. Concluding that biocontrol before harvest does not replace the need for better postharvest practices, since the population of toxigenic *A. flavus* in the harvested grain increased and produced aflatoxins throughout the drying time when the humidity was high [48]. Yerkovich et al. report a reduction in the accumulation of deoxynivalenol of 60% in wheat crops, when *Bacillus velezensis* RC218 was applied, this in greenhouse tests. Although, as they mention, climate change must be considered, when applying combined strategies with fungicides, biocontrol, and cultivars to control the accumulation of mycotoxins [103]. Finally, Table 4 describes other studies carried out to evaluate the detoxification of the main mycotoxins that contaminate food. These methods have proven to be a useful alternative for the control of mycotoxins, which can also be friendly to the environment. Likewise, Table 5 mentions some of the methodologies used for the identification and control of mycotoxigenic fungi.

Conclusion

The impact of climate change is affecting the agri-food system, generating optimal conditions for the proliferation of mycotoxigenic fungi. Environmental factors such as temperature and relative humidity, as well as agricultural practices, contribute to the production of mycotoxins. The foregoing makes this a topic of relevance worldwide since the control of these fungi and their metabolites compromises food safety. One of the most visible effects is the decrease in productivity, and therefore in the supply of food for both human and animal consumption. Even the poor quality of food contaminated by these metabolites affects human and animal health. These are friendly to the environment since the use of chemical fertilizers as a control measure destroys the ecological environment of the soil and can generate resistance. Detection methods for mycotoxins in food and feed must be fast, cheap, sensitive, and selective. Detection proposals include ELISA, ULISA, MSMA, aptasensors, and biosensors. Among the control measures that can become effective alternatives for detoxification are the use of natural extracts, essential oils, ultraviolet irradiation, co-cultures, and biodegradation. All these methods are a useful alternative to guarantee safe food, of good quality and sufficient for consumption demands.

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Table 4: Mycotoxin control strategies.

Micotoxins	Control strategies	Results	References
AFB1	Aqueous extracts *Passiflora alata, Psidium cattleianum, Rosmarinus officinalis* and *Origanum vulgare*	Reduction from 49.0 to 60.3% for *R. officinalis*, *O. vulgare* with 38.3% and *P. cattleianum* with 30.7%	[78]
AFB1, FB1	CAPP	Concentration reduction of up to 66% in corn for AFB1 and FB1	[98]
DON	Use of gaseous ozone, UV-C radiation, and CA	Degraded more than 90% of AFB1 and AFB2 and more than 99% of AFG1 and AFG2	[9]
Toxina T2, ZEN, FB1, FB2	Biodegradation of a collection of *Bacillus megaterium* BM344-1 and *B. pumilus* BP344-3	BM344-1 and BP344-3 showed 100% degradation of ZEN in *Luria Bertani* (LB) liquid medium. BM344-1 degraded FB1 and FB2 by 14 and 12%, respectively.	[32]
ZEN	*Candida parapsilosis* ATCC 7330	Level of ZEN (20 µg/mL) decreased by 97%	[73]
DON	Biological treatment using *Lactobacillus* fermentation	*L. uvarum* allowed to reduce the DON content in wheat-based products up to 75%	[92]
AFB1	Ultraviolet irradiation of the C region	AFB1 reduction in corn ranged from 17 to 43% and in peanuts from 14 to 51%	[93]
AFB1	Co-culture of *Aspergillus niger* and *Pleurotus ostreatus*	93.4% of AFB1 degradation	[96]
AFB1	Ratiometric surface-enhanced Raman scattering	Limit of detection was as low as 0.1 pg/mL	[21]
DON, beauvericin.	UHPLC–MS–IT–TOF	Occurrence in more than 82% of the samples	[31]

CAPP: Cold Atmospheric Pressure Plasma; CA: citric acid; UHPLC–MS–IT–TOF: ultra-high-performance liquid chromatography coupled to mass spectrometry–ion trap–time-of-flight.

Table 5: Detection and control of mycotoxigenic fungi.

Control strategies	Results	References
PeAfpA	*Alternaria, Aspergillus, Byssochlamys, Fusarium*, and *Penicillium* were inhibited by concentrations ranging from 0.5 to 16 µg/mL	[60]
PCR	Of 227 isolates, *Aspergillus* made up 54.9%, *Penicillium* 23.3% and Fusarium 14.3%.	[1]
qPCR	LOD95: 123.5 spores/50 g and 37.1 spores/50 g for 24 h and 48 h respectively.	[81]
NaMBS	No growth of *A. flavus* occurred with > 500–1250 NaMBS mg/l	[5]
LAB	Inhibition against *A. flavus* F008BA by *L. fermentum* 5KJEU5 (9.06%)	[68]
LAB	*Lactiplantibacillus plantarum* inhibited the growth of *Penicillium* spp.	[59]
(E)-2-hexenal	4.0 µL/mL (MFC) of (E)-2-hexenal induced a 38.4% rate of early markers of apoptotic cell death in *A. flavus* conidia	[56]
Stilbenes	Pterostilbene with methoxy had the best antifungal properties, followed by piceatannol, and resveratrol.	[17]

ITS1: internal transcribed spacer 1; ITS4: internal transcribed spacer 4; qPCR: quantitative real-time PCR; NaMBS: sodium metabisulphite; LAB: antifungal lactic acid bacteria; MFC: minimum fungicidal concentration.

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