agronomy

MDPI

Perspective

How Maize Seed Systems Can Contribute to the Control of Mycotoxigenic Fungal Infection: A Perspective

P. Christiaan Biemond [1,2], Tjeerd Jan Stomph [2], P. Lava Kumar [3] and Paul C. Struik [2,*]

[1] International Institute of Tropical Agriculture (IITA), IITA-Kano, PMB 3112, Sabo Bakin Zuwo Road, Kano 713103, Nigeria; christiaan.biemond@wur.nl
[2] Centre for Crop Systems Analysis, Plant Sciences Group, Wageningen University, P.O. Box 430, Bornsesteeg 48, 6708 PE Wageningen, The Netherlands; tjeerdjan.stomph@wur.nl
[3] International Institute of Tropical Agriculture (IITA), PMB 5320, Oyo Road, Ibadan 20001, Nigeria; l.kumar@cgiar.org
* Correspondence: paul.struik@wur.nl; Tel.: +31-317-484246

Abstract: Mycotoxins are toxic secondary metabolites produced by fungi on agricultural produce. Mycotoxins can be cytotoxic, genotoxic, mutagenic, and teratogenic, and they are persistent threats to human and animal health. Consumption of mycotoxin-contaminated maize can cause cancer and even sudden death. Health hazards can also occur from consuming products from animals fed with mycotoxin-contaminated feed or forage. The main mode of spread of mycotoxigenic fungi is through air-borne spores originating from soil or plant debris, although some fungi can also spread through infected seed-to-seedling transmission, ultimately followed by contamination of the harvestable product. This perspective assesses opportunities to prevent mycotoxigenic fungal infection in maize seeds produced for sowing as an important starting point of crop contamination. A case study of Nigeria showed infection in all tested farmer-produced, seed company, and foundation seed samples. A schematic overview of the formal and informal seed systems is presented to analyze their contribution to fungal infection and mycotoxin contamination in the maize value chain, as well as to set criteria for successful control. We recommend an integrated approach to control mycotoxigenic fungal infection, including resistant varieties and other control methods during seed production, grain production, and grain storage, with an important role in maintaining seed health.

Keywords: *Fusarium verticillioides*; mycotoxigenic fungi; mycotoxins; seed systems; sub-Saharan Africa; *Zea mays*

Citation: Biemond, P.C.; Stomph, T.J.; Kumar, P.L.; Struik, P.C. How Maize Seed Systems Can Contribute to the Control of Mycotoxigenic Fungal Infection: A Perspective. *Agronomy* **2021**, *11*, 2168. https://doi.org/10.3390/agronomy11112168

Academic Editors: Carla Ceoloni, Silvio Tundo and Ljiljana Kuzmanović

Received: 30 August 2021
Accepted: 25 October 2021
Published: 28 October 2021

1. Introduction

1.1. Background

Mycotoxins are secondary metabolites produced by certain types of fungi, such as *Alternaria*, *Aspergillus*, *Fusarium*, and *Penicillium* spp., on agricultural produce, such as maize (*Zea mays* L.). Mycotoxins enter the food chain as results of preharvest and postharvest fungal infection. These mycotoxins are an important health hazard in developing countries, such as those in sub-Saharan Africa, which is receiving little but growing attention [1–5].

Most hazardous mycotoxins in human foods or animal feeds in sub-Saharan Africa include aflatoxins, ochratoxins, fumonisins, deoxynivalenol, and zearalenone [2,4]. These mycotoxins are very stable and, therefore, can remain present during crop production and harvest, during transport and storage, and even during processing and postprocessing events [2]. They also accumulate in animal products from animals fed with contaminated feed or forage [5].

Chronic exposure to mycotoxin-contaminated maize can cause cancer, while acute exposure can lead to sudden death [6]. Mycotoxin exposure is most common in developing countries with poor food handling, inadequate food storage, malnutrition, and weak

regulations to prevent entry of food and feed products with mycotoxins beyond permissible limits for consumption [7].

Given the negative impacts of these fungal toxins, the mycotoxins have a large impact on nutrition security and livelihood, as well as affect the competitiveness of agricultural production in sub-Saharan Africa [2]. Despite increasing awareness of the problem, in many cases, the contamination with mycotoxins still exceeds the maximum tolerable threshold levels and, thus, continues to threaten public health [2]. Possible solutions for this health hazard are capacity building and value chain management.

However, for control of mycotoxins, the value chain is complicated and should not be taken lightly. For example, Kamika et al. [8] described the occurrence of aflatoxin contamination in maize throughout the food supply chain in the Democratic Republic of Congo. They demonstrated that aflatoxins are ubiquitous; in the preharvest period, 16 out of 50 samples tested were positive for aflatoxins. However, as the supply chain progressed, the contamination with aflatoxins went up, both in frequency and in intensity, until 100% of the collected maize samples contained aflatoxins at levels that were 300 times higher than the maximum limit of 10 μg/kg set by the World Health Organization [8]. Maximum levels observed at the end of the supply chain (in shops and on markets) were as high as 500 times this maximum tolerable level.

However, similar hazards can occur by consuming animal products in which mycotoxins have accumulated. Gruber-Droninger et al. [4] collected 74,821 samples of feed or feed raw materials from 100 countries across the globe during a period from 2008 until 2017 and analyzed these samples for various mycotoxins. They demonstrated that 88% of the samples were contaminated with at least one mycotoxin and many samples exceeded the health standards. However, they also observed large differences among regions and significant year-to-year variation in occurrence of mycotoxins in animal feed. These differences were very much related to climatic and weather factors, especially rainfall and temperature during sensitive phases of feed and forage production.

These findings cry for a stricter control of mycotoxins, but also suggest that it is not easy under the changing global conditions to maintain control over mycotoxins (see also [9]). Marroquin-Cardona et al. [9] made a plea to balance global mycotoxin standards with what they called "a realistic feasibility of reaching them, considering limitations of producers".

High-income countries control the mycotoxin hazard with a combination of regulation and certification (Figure 1A). The Food and Drug Administration (FDA) [10] and the European Commission [11,12] determined maximum food contamination levels for specific mycotoxins to protect consumers from mycotoxin exposure. Certifications, such as the Hazard Assessment and Critical Control Point (HACCP), assist companies in the food value chain to prevent mycotoxin contamination and keep it within acceptable levels [13]. However, certification and enforcing food regulations are not compatible with smallholder farming and local or regional value chains in low-income countries [4,5,8,9], such as countries in sub-Saharan Africa. Farmers consume part of their own produce without market interference, making food safety control difficult to execute [6], while locally sold and purchased grains are also not covered by such controls.

Moreover, in many countries of sub-Saharan Africa, there is a substantial amount of regulation and legislation on the control of mycotoxins but without effective enforcement and oversight [2]. There is also a limiting economic factor: food safety controls would increase food prices where the majority of the population already spends up to 50% of their income on food [14].

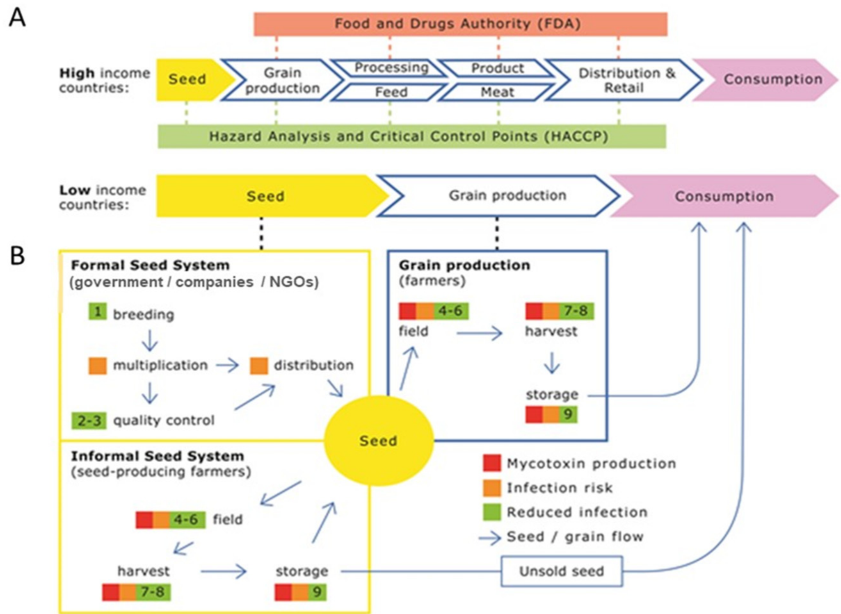

Figure 1. (**A**) Maize value chains in high- and low-income countries. Regulation by, e.g., the FDA and certifications such as HACCP avoid mycotoxin contamination in maize in high-income countries. Low-income countries lack sufficient regulations or implementation systems to avoid mycotoxin contamination in maize. A relatively large share of the maize production is consumed without industrial processing, resulting in a shorter value chain compared with the chains in high-income countries. (**B**) An idealized picture of the effects of formal and informal seed systems on mycotoxigenic fungal infection, mycotoxin production, and control methods in low-income countries. The formal seed system consists of government bodies, NGOs, and private companies involved in breeding, seed multiplication, external quality control, and dissemination of seed, while the informal seed system only consists of seed-producing farmers. In the formal seed system, contamination should not occur as seed health is maximized and seed treatment is standard practice to avoid survival of any possible pathogen, including mycotoxigenic fungi. Our case study (see text) demonstrates that a suboptimally functioning formal seed system may also result in seed stocks with some contamination. Arrows show flows of maize seed or grain. Control methods to avoid or reduce mycotoxigenic fungal infection include breeding insect- and mycotoxigenic fungi-resistant varieties (1), seed health testing (2), seed treatment with fungicides or biological control agents (3), atoxigenic strains (4), agrochemical application (5), biological control (6), avoiding seed damage (7), fast drying to <14% moisture (8), and clean and dry storage (9). An important question remains whether mycotoxin-producing fungi are ubiquitous in soils where maize is grown.

An important control strategy to avoid mycotoxin contamination is to prevent toxigenic fungal infection, including genetic and agronomic approaches [15]. If awareness of the hazards is present, knowledge on control measures is available, and proper incentives are in place to carry out the proper measures, then it is possible to reduce the problem. However, an often ignored part of the supply chain and an overlooked part of the "contamination chain" is the seed production preceding the production of the marketable food or feed. It has been reported that mycotoxin contamination can start as seed-to-seedling transmission from infected seeds, resulting in infected plants and infested produce [16]. If this is a significant route of contamination, then the seed system should be taken into account as part of the supply chain. This research, therefore, proposes a conceptual framework to assess contributions of formal and informal seed systems to the propagation of the contamination with mycotoxins. We also analyze how seed health can be controlled to avoid or reduce mycotoxigenic fungal infection in developing countries.

Data on current mycotoxin threats in maize value chains in sub-Saharan Africa are rare and rather unbalanced between countries. Important research groups have published

relevant datasets for countries such as Benin [5], Cameroon [5], Congo [3,8], Kenya [17,18], Mali [5], Nigeria [1,5,19], and South Africa [20]. For other countries identified by FAO statistics as growing maize as a major staple or feed crop on a large scale, e.g., Mozambique, Tanzania, Uganda, and Zimbabwe, such datasets are not to be found. The fact that just a few countries are mentioned in the reviewed literature is a reflection of the activity of research groups and, therefore, available literature rather than an indication of the extent of the problem. There are no reasons to assume the problem is smaller in other countries in sub-Saharan Africa (see, e.g., [2,4,5]) or in other developing economies across the globe with comparable institutional settings. The latter is confirmed by research reports from Haiti [21,22], Iran [23], and China [24,25]. In Haiti, aflatoxins were present in 55% of the maize kernel samples [21], but the frequency of infection strongly depended on locality and, therefore, on farming system, storage system, and weather conditions [22]. In Iran, a large diversity of *Fusarium* species was observed on maize kernels, and this diversity increased the risk of multi-toxin contamination, thus enhancing the risk of health hazards for humans and animals [23]. In China, a great diversity of *Fusarium* species was also found in maize kernels; however, this diversity depended on the region of origin of the samples [24]. In China, co-occurrence of various mycotoxins occurred in 60% of the maize kernel samples [25], thus increasing health risks. However, in high-income countries, issues with mycotoxins might also arise, e.g., in Belgium [26], Germany [27], and Spain [28]. In Belgium, it was observed that every maize silage, used for winter feed of dairy cattle, was contaminated with at least two different mycotoxins [26]. In Germany, researchers proved that infection of the maize crop could occur throughout the growing season, causing various types of diseases in vegetative and reproductive organs; *Fusarium* ear rot was particularly important for the toxigenic quality of ear-based maize products [27]. Lastly, in Spain, it was demonstrated that *Fusarium* could be transmitted through seed in very diverse agricultural and horticultural crops, including ornamentals [28].

In this paper, a case study from northern Nigeria is used to illustrate the infection levels of locally available maize seed as important risk factors in the "contamination chain". A schematic overview of the seed system is presented to analyze the problem of mycotoxigenic fungal infection of seed. Potential control methods are discussed in relation to sustainable implementation in the formal and informal seed systems.

1.2. Mycotoxins

Mycotoxins are defined as natural products with low molecular weight, produced as secondary metabolites by filamentous fungi. They are toxic to vertebrates in low concentrations and differ widely in biosynthetic origin, chemical structure, and toxicity [7,17,18,20,26,29,30]. The symptoms of mycotoxin poisoning depend on the type and amount of mycotoxin, duration of exposure, and the age, sex, health, and nutritional status of the victim [7,18]. An example of fatal mycotoxin poisoning was the aflatoxicosis outbreak in Kenya in 2004. Over 300 people got acute hepatic failure after consumption of aflatoxin-contaminated maize, which eventually killed 125 people [31]. However, the literature not only reports on contaminated food, but also puts emphasis on the contamination of animal feed with mycotoxins and the subsequent contamination of animal products [17,20,29].

The most prevalent fungi that can produce mycotoxins belong to the genera *Alternaria*, *Aspergillus*, *Fusarium*, and *Penicillium*. Control measures differ in effectiveness between genera. Avoiding grain damage during harvest, fast drying to low moisture levels, and adequate storage methods can be effective against *Alternaria* and *Aspergillus* species. These "storage fungi" produce mycotoxins primarily during storage, in contrast to *Fusarium* and *Penicillium* species which produce mycotoxins mostly under field conditions [32].

Optimal storage conditions do not solve the problem of preharvest mycotoxin production; anyway, they are difficult to implement for developing countries. Agronomic practices such as crop rotation, tillage, irrigation, and fertilizer application do not provide sufficient protection either, and available varieties do not have sufficient levels of resistance against all mycotoxigenic organisms. Mycotoxigenic fungal infection in maize is a persistent prob-

lem in developing countries [15]. Especially *Fusarium verticillioides* (Sacc.) Nirenberg is problematic. This fungus is a seed-borne species in maize and results in systemic infection in the plant. Neither seed treatments with fungicides nor chemical control in the field are suitable control measures under the conditions of smallholder farmers, for example because these farmers may not have access to these chemical crop protectants or cannot afford such treatments, or because they may not have enough yield incentives to warrant the application of such treatments, while not being awarded for keeping their produce mycotoxin-free. Biological control strategies are developed involving pre- or postharvest applications of biocontrol agents [16]. Such strategies could involve biopriming of the seeds with *Trichoderma harzianum* Rifai [33–35], *T. gamsii* Samuels & Druzhin. [36], or *Pseudomonas fulva* Iizuka & Komagata [37].

As it is unlikely that resource-poor farmers will pay for an extra treatment without benefits such as higher yield or increased market price for mycotoxin-free maize [3], biocontrol should always have multiple effects. Seed health is not only an important aspect in the control of *F. verticillioides*, but can also contribute to the control of other seed-borne, mycotoxigenic fungi, e.g., *Fusarium oxysporum* Schlecht. emend. Snyder & Hansen, *Fusarium solani* (Mart.) Sacc., and *Penicillium oxalicum* Currie, J.N.; Thom, C. [38].

1.3. Informal and Formal Seed Systems

Seed health, i.e., the absence of any pathogens causing seed deterioration or plant diseases after germination, can only be controlled through the source of seed, i.e., the seed system [39]. A seed system can be defined as all activities related to seed production, seed storage, seed management, seed dissemination, and seed use. A sustainable seed system can ensure that high-quality seeds of a wide range of varieties and crops are produced and fully available in time and affordable to farmers and other stakeholders. In the literature, a distinction is made between "formal seed systems" and "informal seed systems". The latter are also called "local seed systems", "farmers' seed systems", or "traditional seed systems".

The formal seed system consists of government bodies, NGOs, and private companies involved in breeding, seed multiplication, external quality control, and dissemination of seed (Figure 1B) [40]. Seed certification is an essential part of the formal seed system. Government bodies and NGOs run public breeding programs, while some seed companies also develop new varieties. Responsible authorities test varieties for Distinctness, Uniformity, and Stability (DUS) criteria for varietal registration. The new varieties are multiplied, tested for seed quality, certified, and sold to farmers.

The informal seed system consists of farmers, usually smallholder farmers, producing seed for their own use, and often selling or exchanging seed within their local community, including neighbors, friends, families, or even local markets [40–44]. There is no formal oversight in informal seed systems. Informal seed systems are often more flexible and diverse, accepting or even creating more genetic diversity (such as mixtures, landraces). Nevertheless, in general, farmers try to maintain some level of purity and seed quality, but they are not able to test it. Excess seed is used for own consumption or sold as grain on the market. Therefore, seed and grain (or seed and ware) often cannot be clearly distinguished.

Both seed systems interact. The informal seed system depends on the formal seed system to access new varieties and for occasional seed renewal, while the formal seed system uses the informal seed system for farmer participatory breeding, sourcing additional genetic diversity, varietal testing, or seed multiplication [42–44]. Farmers involved in grain production can buy seed from the formal seed system for a relatively high price, purchase seed locally from the informal seed system for a relatively low price [44], or recycle seed for several years, before replenishing from other sources.

Using locally produced seed or recycling one's own seed can result in a buildup of mycotoxigenic fungi in the seed, provided such fungi are present in the fields in the area. Seed treatment of local or recycled seed can improve seed health and, therefore, mitigate the contamination with mycotoxins, but will only be implemented if it coincides with other

incentives, such as higher yields or better quality of food, feed, or animal products, as already indicated above.

2. Maize Seed Health in Nigeria

2.1. Maize Seed Systems

Since the informal seed system lacks access to required infrastructure, seed-producing farmers do not test seed health, despite being very aware of the risks of seed-borne diseases [3]. Recent research results from Nigeria showed that farmer-produced seed samples were heavily infected with a range of mycotoxigenic fungi [45]. All samples were infected with *Fusarium verticillioides* with a median infection incidence of 55.2% (Table 1). The fungus can produce fumonisins that are classified as potentially carcinogenic to humans causing esophageal cancer. Avoiding fumonisin contamination may prevent 1,000,000 HIV transmissions in sub-Saharan Africa annually [46]. The most frequently occurring *Aspergillus* fungus was *Aspergillus niger* van Tieghem, occurring in 61% of the samples, which can produce the mycotoxins ochratoxin A (OTA) and fumonisin B2 [47]. Ochratoxin A is classified as possible human carcinogen and shows immunotoxic properties [48]. *Penicillium oxalicum* was identified in 29% of farmer-produced seed samples. The fungus can produce the mycotoxin secalonic acid D [49], which dramatically increases the chance of cleft palate, a common birth defect [50]. Soil-borne *Aspergillus flavus* Link, producing aflatoxins, occurred in 38% of the farmer-produced seed samples. Chronic aflatoxin exposure can lead to stunted growth of children, liver cancer among adults, and reduced life expectance, while acute aflatoxicosis can be lethal within weeks [6]. The seed company and foundation seed samples were also heavily infected with various mycotoxigenic fungi (Table 1) [45]. The fact that mycotoxigenic fungi appear in seed company samples raises the question whether seed treatment should be made mandatory to control seed-borne mycotoxigenic fungi.

It should be noted that control of mycotoxigenic fungi does not stand alone. Chalivendra et al. [51] demonstrated that there is a strong interaction with insect damage. Lowering mycotoxin levels might actually increase insect damage. This stresses the need for integral pest and disease management strategies in seed systems and complicates breeding for resistance against mycotoxigenic fungi and subsequent variety selection. On the other hand, breeding for increased levels of phlobaphenes in the seed could be a powerful strategy to improve grain quality by reducing mycotoxin accumulation [52]. Breeding for such varieties might limit the spread of seed-borne mycotoxigenic fungi through seed systems in the "mycotoxin chain". Lastly, Gao et al. [53] reported on opportunities to make use of antagonistic mechanisms against *Fusarium verticillioides* enhancing seed health by stimulating the endophyte *Sarocladium zeae* (W. Gams & D.R. Sumner) Summerbell.

Table 1. Overview of mycotoxigenic fungi identified in maize seed samples obtained from farmers (*N* = 87), a seed company outlet (*N* = 6), and a foundation seed producer (*N* = 6). Samples were collected in 2009 and 2010 in Nigeria. Fungal growth in each sample was determined for 500 undamaged, surface sterilized seeds after 4 days of incubation on agar. The infection frequency, i.e., the percentage samples with at least one infected seed, and the median infection incidence, i.e., the median of the percentage of seeds infected per sample based on infected samples only, are shown for seed samples from farmers, a seed company, and a foundation seed producer.

			Farmers (*N* = 87)		Seed Company Outlets (*N* = 6)		Foundation Seed Producer (*N* = 6)	
Mycotoxigenic fungi	**Mycotoxins Produced ****	**Seed-Borne**	**Infection Frequency (%)**	**Infection Incidence (%)**	**Infection Frequency (%)**	**Infection Incidence (%)**	**Infection Frequency (%)**	**Infection Incidence (%)**
Aspergillus flavus	Aflatoxin [a]	U [e]	38	0.6	17	0.8	83	0.4
Aspergillus niger	Ochratoxin A [b]	Y [e]	61	0.6	83	0.6	100	1.0
Fusarium oxysporum	Deoxynivalenol [c]	Y [e]	53	1.4	67	5.1	33	3.8
Fusarium solani	Deoxynivalenol [c]	Y [e]	5	0.9	0	- ***	17	0.8
Fusarium verticillioides *	Fumonisins [a]	Y [e]	100	55.2	100	48.7	100	45.1
Penicillium oxalicum	Secalonic acid D [d]	Y [e]	29	0.6	50	0.2	67	1.4

* Synonym: *Fusarium moniliforme* Sheldon. ** [a] [54]; [b] [47]; [c] [55]; [d] [49]; [e] [38]; U = unlikely, Y = yes. *** No organism identified in samples. Data are derived from [45].

The results of maize seed were compared with maize grain meant for consumption. Several studies collected maize samples from local markets in African countries and analyzed fungal infection. The dominance of *F. verticillioides* infection in Nigerian maize was confirmed in these reports [56]. Evidence from southwest Nigeria showed a maize grain infection frequency of 89.3% and an infection incidence of 49.4% for *F. verticillioides*, while infection incidences of other identified fungi varied from 1.3–14.7% [57]. The seed samples of the current research showed similar results with high infection frequency (100% of farmer produced seed) and incidence (55.2%) for *F. verticillioides*, in combination with low infection incidences for all other identified fungi. The list of identified fungi differed between southwest and northern Nigeria [45], probably due to environmental differences. Maize grain samples in South Africa showed similar infection levels of *F. verticillioides* (identified in 87.5% of the samples), *A. flavus* (42.5%), *A. niger* (25.0%), and *P. oxalicum* (27.5%) [58]. It appears that seeds have similar infection levels compared with maize grain meant for human consumption.

2.2. Relevance of the Different Fungi

Although the seed samples were not tested for mycotoxins, it is highly unlikely that the identified fungi solely contain atoxigenic strains. Atoxigenic strains are not able to produce mycotoxins, in contrast with toxigenic strains. Results from Portuguese maize showed that 14% of the *A. niger* isolates could produce ochratoxin A and 39% fumonisin B [59], while a report of maize in Argentina showed that 25% of the *A. niger* strains were toxigenic [60]. A search for atoxigenic *A. flavus* strains in Kenya showed that only 33% of the analyzed isolates were atoxigenic, while the majority could produce aflatoxins [61]. An experiment in Kansas, USA, could not identify any atoxigenic strains of *F. verticillioides*, and isolates with relatively low fumonisin production in vitro did not show a consistently low level of fumonisin production in vivo [54]. All four cases have in common that atoxigenic strains were absent or accompanied by toxigenic strains, leaving the risk of mycotoxin production. Another aspect to judge the relevance of the identified fungi is their ability to transmit the fungus from seed to seedling, so-called seed-borne pathogens. Seed-borne infections are an important infection source for *F. verticillioides* [16]. The other two *Fusarium* species, *A. niger* and *P. oxalicum*, are also seed-borne diseases, but *A. flavus* is most likely only soil-borne or occurs as a surface contaminant [38].

3. Control

3.1. Control Methods

The case study of maize seed in Nigeria showed that both formal and informal seed systems struggle with mycotoxigenic fungal infection, but there are several control methods that can reduce infection. Important control methods of the formal seed system are integrated approaches, including postharvest processing and storage methods, seed health testing to test and avoid heavily contaminated stocks and prevention through resistant varieties (breeding) where available, and application of biocontrol methods (use of atoxigenic strains and antagonists). However, seed companies may not have the infrastructure themselves or cannot charge higher seed prices to cover seed health testing costs. Breeding programs have reported sources of resistance against *A. flavus* preventing aflatoxin contamination [62] and against *F. verticillioides* preventing fumonisin production, but varieties resistant to all mycotoxigenic fungi are currently not available [63]. Insect resistance is also a valuable trait to avoid infection, because insect damage facilitates the entry of fungi into and subsequent infection of maize plants [8]. Farmers may easily adopt these varieties when combined with other beneficial traits such as tolerance to low soil fertility and drought, resistance to the parasitic weed *Striga* spp., or higher market value of the product. Research is already going on to optimize the dissemination of improved varieties by the formal and informal seed systems [44], as well as increase adoption of improved maize varieties by smallholder farmers [64,65]. However, earlier in this paper, we reported that there is a tradeoff between lowering the mycotoxin level and reducing insect damage [51].

The growing season offers ample opportunities to farmers, seed companies, and foundation seed producers to avoid mycotoxigenic fungal infection. Seed treatment with fungicides might reduce infection with *A. flavus* and *A. niger*, as well as simultaneously enhance germination [66], but whether it can stop seed-to-seedling transmission of *F. verticillioides* is debated [16]. Another control method is foliar agrochemical application which may not be feasible to smallholder farmers and may not be ecofriendly. Insecticides reduce insect damage to the plant, preventing airborne spores of mycotoxigenic fungi such as *F. verticillioides* from entering and infecting the plant. A combination of insecticide and fungicide can reduce infection with *F. verticillioides*, Fusarium ear rot incidence, and fumonisin contamination [67].

Although agrochemicals can enhance yields and production quality, high costs and adverse health effects for farmers can hamper the adoption. Biological control agents form an alternative to agrochemicals. Preharvest application of *Bacillus subtilis* avoids fumonisin production, because the biocontrol agent competes for the same niche as *F. verticillioides* [16]. Another biological control method is the application of atoxigenic strains of *A. flavus* to the soil surface. The atoxigenic strains colonize the soil, infect the plant, and compete for the same niche with toxic *A. flavus* strains [61]. A similar strategy might be feasible with atoxigenic *Fusarium* spp. strains to combat mycotoxigenic *Fusarium* spp. [68]. In addition to effectiveness against mycotoxins, biological controls lack additional benefits that lead to a financial incentive for farmers, which will most likely hamper adoption. Harvest and storage practices also form potential control options. Avoiding seed damage during harvest can avoid further fungal infection.

There are also ample opportunities to control mycotoxigenic fungi post harvest [1,19]. Fast drying of maize after harvest to a final moisture content <14% is important to prevent fungal growth during storage [1] but can be difficult to achieve in humid areas with labor scarcity at harvest time. Creating optimal storage conditions with low humidity, protection against insects, and an absence of infected plant material can avoid new infection [69]. For seed, hermetic storage bags are potentially relevant. The use of PICS bags provides a good option [70]. The use of plant extracts or essential oils and other natural compounds during storage to reduce infection has been widely investigated and recommended [71–74]. However, it is questionable whether smallholder farmers have the resources to treat seed differently from grain. Nevertheless, it is important to educate these farmers about the risks and possible routes of contamination and possible control strategies [1].

It is important to design a set of good practices during the entire supply chain with balanced attention for conditions and practices during primary production, including crop rotation, use of fungicides and insecticides, use of resistant varieties, and careful harvesting and conditions and practices after harvesting, as well as during storage, processing, and marketing, equally paying attention to mass flow and information flow. However, we make a plea to take the production, storage, and use of seed into account and not merely focus on the production of food, feed, or forage.

In addition to seed treatments based on chemical fungicides, there is a growing body of literature showing options to treat seeds using biological control agents. Work on strains of the fungus *Trichoderma harzianum* has shown promise both in the lab [33,34,36,75] and in the field [33,35]. Moreover, strains of bacteria from the genera *Pseudomonas* and *Lactobacillus* have been found to reduce contamination either in the field (contamination of *Fusarium* [37]; contamination of *Aspergillus* [76]) or post harvest (contamination of *Aspergillus* [77]). Much more field work under soil and disease pressure conditions typical to smallholder farmers in low- and middle-income countries will be needed, and input value chains will need to be developed. An important under-researched aspect is what the direct economic benefits of such seed treatments would be for smallholder farmers with different resource endowments in low- and middle-income countries, as consumer health including their own is not a sufficient incentive for seed treatment [2,3].

3.2. Adoption Constraints

Adoption of these control strategies in sub-Saharan Africa is constrained by a lack of financial incentives and lack of awareness of the health hazard. Farmers and consumers cannot discriminate between mycotoxin-contaminated maize samples and a safe product by visible inspection [78], making it highly unlikely that contaminated maize samples are sold for lower prices. Therefore, there is no financial incentive for farmers to invest in avoiding or reducing mycotoxin contaminations. Even if there was a clear financial incentive, socioeconomic constraints could still hamper adoption by smallholder farmers, as what happened for fertilizer application [79].

Another aspect is the sustainable implementation of control measurements in the seed systems. To inform millions of smallholder farmers in remote areas and convince them to make financial investments in control methods might be the biggest constraint of the informal seed system. The formal seed system consists of a relatively small number of actors, but adoption may be constrained by weak government institutions, development and enforcement of regulation, and market failure. At the same time, if farmers are using self-saved seeds (i.e., recycled seeds), simultaneous intervention in their seed production and grain production might be relatively easy and productive, once awareness has been created. Further development of biocontrol systems that can be based on locally produced antagonists or biorationals and enhance both productivity and quality is worth investigating. These could turn out to be low-cost and locally reproducible systems. These developments can be supported by stakeholders as there is some prospect of awareness, followed by action, as demonstrated by [2], as smallholder farmers are not merely driven by financial incentives.

Successful control strategies against mycotoxigenic fungal infection combine (a) effectiveness, (b) additional financial benefits beyond mycotoxigenic fungi prevention, and (c) easy and sustainable implementation in seed systems. Breeding resistant varieties is an important control method meeting these three criteria. Seed treatments, agrochemical spraying, avoiding seed damage at harvest, and storage technologies only meet the two criteria (effectiveness and additional financial benefits), but encounter important implementation problems in seed systems. Application of biological control or atoxigenic strains is effective and may have additional financial benefits, but is difficult to implement in a seed system. However, the use of biocontrol options deserves to be further explored and exploited.

3.3. Integrated Approach

Mycotoxins are here to stay and, therefore, we need to set strict control regimes and regulations [9]. We recommend an integrated approach to develop optimal mycotoxigenic fungal infection control. This approach consists of mycotoxigenic fungi- and insect-resistant varieties in combination with effective control measures during seed production, grain production, and storage that also have additional financial benefits beyond mycotoxin control and are in balance with measures preventing insect damage. Proper drying after harvest and improved storage methods should certainly be part of the integrated approach, e.g., through the use of hermetic storage bags such as PICS bags. If mycotoxigenic fungal control is still insufficient, other effective control measures can also be applied, even when they do not provide additional benefits other than control of mycotoxigenic fungi. The optimal mix may differ among regions and countries as a result of agroecological, socioeconomic, and sociopolitical differences. This strategy might also be relevant for mycotoxin contamination in other crops. Further research is recommended to test combinations of control measurements for different climatic zones, crops, and countries, as well as test their effectiveness, additional financial benefits, and sustainable implementation in the seed system. Public research programs are recommended to breed mycotoxigenic fungi resistance into varieties popular among farmers and to develop new methods to control mycotoxigenic fungal infection.

4. Conclusions and Recommendations

Mycotoxin-contaminated maize is a known human health hazard in developing countries, but the potential link between infected seed and preharvest infection is understudied. Similarly, a seed system approach to control this hazard requires more research. Maize seed samples are heavily infected with mycotoxigenic fungi, as illustrated by the Nigerian case study. A schematic overview of the formal and informal seed systems was presented to visualize the risks of mycotoxigenic fungal infection and mycotoxin contamination, as well as potential control measures. We recommend an integrated approach combining resistant varieties with other methods to prevent mycotoxigenic fungal infection, with special attention to sustainable integration in formal and informal seed systems. Further research is recommended to determine the optimal combination of control measures for different climate zones, socioeconomic conditions, and crops, as well as to breed varieties with resistance to all mycotoxigenic fungi.

Author Contributions: Conceptualization, P.C.B., T.J.S., P.L.K., and P.C.S.; methodology, P.C.B.; validation, P.C.B.; formal investigation, P.C.B.; resources, P.C.B., T.J.S., P.L.K. and P.C.S.; data curation, P.C.B.; writing—original draft preparation, P.C.B., T.J.S. and P.C.S.; writing—review and editing, P.C.B., T.J.S., P.L.K. and P.C.S.; visualization, P.C.B.; supervision, T.J.S. and P.C.S.; project administration, P.C.B. and P.L.K.; funding acquisition, P.C.B., T.J.S., P.L.K. and P.C.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Onyeche, V.; Umeh, E.U.; Gberikon, G.M.; Ogbonna, I.O. Determination of fungal population in maize grains from Benue State Nigeria. *Appl. Microbiol. Open Access* **2021**, *7*, 190.
2. Udomkun, P.; Wiredu, A.N.; Nagle, M.; Bandyopadhyay, R.; Müller, J.; Vanlauwe, B. Mycotoxins in Sub-Saharan Africa: Present situation, socio-economic impact, awareness, and outlook. *Food Control.* **2017**, *72*, 110–122. [CrossRef]
3. Udomkun, P.; Wossen, T.; Nabahungu, N.L.; Mutegi, C.; Vanlauwe, B.; Bandyopadhyay, R. Incidence and farmers' knowledge of aflatoxin contamination and control in Eastern Democratic Republic of Congo. *Food Sci. Nutr.* **2018**, *6*, 1607–1620. [CrossRef] [PubMed]
4. Gruber-Dorninger, C.; Jenkins, T.; Schatzmayr, G. Global mycotoxin occurrence in feed: A ten-year survey. *Toxins* **2019**, *11*, 375. [CrossRef]
5. Ingenbleek, L.; Sulyok, M.; Adegboye, A.; Hossou, S.E.; Koné, A.Z.; Oyedele, A.D.; Kisito, C.S.K.J.; Dembélé, Y.K.; Eyangoh, S.; Verger, P.; et al. Regional Sub-Saharan Africa total diet study in Benin, Cameroon, Mali and Nigeria reveals the presence of 164 mycotoxins and other secondary metabolites in foods. *Toxins* **2019**, *11*, 54. [CrossRef]
6. Wild, C.P.; Gong, Y.Y. Mycotoxins and human disease: A largely ignored global health issue. *Carcinogenesis* **2010**, *31*, 71–82. [CrossRef]
7. Bennett, J.W.; Klich, M. Mycotoxins. *Clin. Microbiol. Rev.* **2003**, *16*, 497–516. [CrossRef] [PubMed]
8. Kamika, I.; Ngbolua, K.-T.-N.; Tekere, M. Occurrence of aflatoxin contamination in maize throughout the supply chain in the Democratic Republic of Congo. *Food Control* **2016**, *69*, 292–296. [CrossRef]
9. Marroquín-Cardona, A.G.; Johnson, N.M.; Phillips, T.S.; Hayes, H.W. Mycotoxins in a changing global environment—A review. *Food Chem. Toxicol.* **2014**, *69*, 220–230. [CrossRef]
10. Egmond, H.P. Worldwide Regulations for Mycotoxins. In *Mycotoxins and Food Safety*; Devries, J., Trucksess, M., Jackson, L., Eds.; Kluwer Academic/Plenum Publishers: New York, NY, USA, 2002; pp. 257–269.
11. European Commission. Commission regulation (EC) No 1881/2006. Setting Maximum Levels for Certain Contaminants in Foodstuffs. Official Journal of the European Union. 2006. Available online: http://eur-lex.europa.eu/RECH_naturel.do?ihmlang=eng (accessed on 19 December 2012).
12. European Commission. Commission regulation (EC) No 1126/2007 of 28 September 2007 amending Regulation (EC) No 1881/2006. Setting Maximum Levels for Certain Contaminants in Foodstuffs as Regards Fusarium Toxins in Maize and Maize Products. Official Journal of the European Union. 2007. Available online: http://data.europa.eu/eli/reg/2006/1881/2021-08-31 (accessed on 3 October 2021).
13. Magan, N. Mycotoxin contamination of food in Europe: Early detection and prevention strategies. *Mycopathologia* **2006**, *162*, 245–253. [CrossRef] [PubMed]
14. Bryngelsson, D.K.; Åhlén, A.; Azar, C.; Persson, U.M. The effect of food-price movements on African households. *Int. J. Agric. Res. Gov. Ecol.* **2012**, *9*, 121–146. [CrossRef]

15. Munkvold, G.P. Cultural and genetic approaches to managing mycotoxins in maize. *Ann. Rev. Phytopathol.* **2003**, *41*, 99–116. [CrossRef]
16. Bacon, C.W.; Yates, I.E.; Hinton, D.M.; Meredith, F. Biological control of *Fusarium moniliforme* in maize. *Environm. Health Persp.* **2001**, *109*, 325–332.
17. Kemboi, D.C.; Ochieng, P.E.; Antonissen, G.; Croubels, S.; Scippo, M.-L.; Okoth, S.; Kangethe, E.K.; Faas, J.; Doupovec, B.; Lindahl, J.F.; et al. Multi-mycotoxin occurrence in dairy cattle and poultry feeds and feed ingredients from Machakos Town, Kenya. *Toxins* **2020**, *12*, 762. [CrossRef]
18. Omara, T.; Kiprop, A.K.; Wangila, P.; Wacoo, A.P.; Kagoya, S.; Nteziyaremye, P.; Peter Odero, M.; Kiwanuka Nakiguli, C.; Baker Obakiro, S. The scourge of aflatoxins in Kenya: A 60-year review (1960 to 2020). *J. Food Qual.* **2021**, *2021*, 8899839. [CrossRef]
19. Onyeke, C.C. Review of mycotoxins in foods in Nigeria. *Food Control* **2020**, *118*, 107376. [CrossRef]
20. Changwa, R.; De Boevre, M.; De Saeger, S.; Njobeh, P.B. Feed-based multi-mycotoxin occurrence in smallholder dairy farming systems of South Africa: The case of Limpopo and Free State. *Toxins* **2021**, *13*, 166. [CrossRef] [PubMed]
21. Aristil, J.; Venturini, G.; Maddalena, G.; Toffolatti, S.L.; Spada, A. Fungal contamination and aflatoxin content of maize, moringa and peanut foods from rural subsistence farms in South Haiti. *J. Stored Prod. Res.* **2020**, *85*, 101550. [CrossRef]
22. Aristil, J.; Venturini, G.; Spada, A. Occurrence of toxigenic fungi and aflatoxin potential of *Aspergillus* spp. strains associated with subsistence farmed crops in Haiti. *J. Food Prot.* **2017**, *80*, 626–631. [CrossRef] [PubMed]
23. Fallahi, M.; Saremi, H.; Javan-Nikkhah, M.; Somma, S.; Haidukowski, M.; Logrieco, A.F.; Moretti, A. Isolation, molecular identification and mycotoxin profile of *Fusarium* species isolated from maize kernels in Iran. *Toxins* **2019**, *11*, 297. [CrossRef] [PubMed]
24. Qin, P.W.; Xu, J.; Jiang, Y.; Hu, L.; van der Lee, T.; Waalwijk, C.; Zhang, W.M.; Xu, X.D. Survey for toxigenic *Fusarium* species on maize kernels in China. *World Mycotoxin J.* **2020**, *13*, 213–223. [CrossRef]
25. Yang, X.; Gao, J.; Liu, Q.; Yang, D. Co-occurrence of mycotoxins in maize and maize-derived food in China and estimation of dietary intake. *Food Addit. Contam. Part B Surveill.* **2019**, *12*, 124–134. [CrossRef]
26. Vandicke, J.; De Visschere, K.; Ameye, M.; Croubels, S.; De Saeger, S.; Audenaert, K.; Haesaert, G. Multi-mycotoxin contamination of maize silages in Flanders, Belgium: Monitoring mycotoxin levels from seed to feed. *Toxins* **2021**, *13*, 202. [CrossRef]
27. Oldenburg, E.; Höppner, F.; Ellner, F.; Weinert, J. *Fusarium* diseases of maize associated with mycotoxin contamination of agricultural products intended to be used for food and feed. *Mycotoxin Res.* **2017**, *33*, 167–182. [CrossRef] [PubMed]
28. Blanco, R.; Aveling, T.A.S. Seed-borne *Fusarium* pathogens in agricultural crops. *Acta Hort.* **2011**, *1204*, 161–169. [CrossRef]
29. Adegbeye, M.J.; Reddy, P.R.K.; Chilaka, C.A.; Balogun, O.B.; Elghandour, M.M.M.Y.; Rivas-Caceres, R.R.; Salem, A.Z.M. Mycotoxin toxicity and residue in animal products: Prevalence, consumer exposure and reduction strategies—A review. *Toxicon* **2020**, *177*, 96–108. [CrossRef] [PubMed]
30. Kebede, H.; Liu, X.; Jin, J.; Xing, F. Current status of major mycotoxins contamination in food and feed in Africa. *Food Control.* **2020**, *110*, 106975. [CrossRef]
31. Azziz-Baumgartner, E.; Lindblade, K.; Gieseker, K.; Schurz Rogers, H.; Kieszak, S.; Njapau, H.; Schleicher, R.; McCoy, L.F.; Misore, A.; DeCock, K.; et al. Case-control study of an acute aflatoxicosis outbreak, Kenya, 2004. *Environm. Health Persp.* **2005**, *113*, 1779–1783. [CrossRef] [PubMed]
32. Tsitsigiannis, D.I.; Dimakopoulou, M.; Antoniou, P.P.; Tjamos, E.C. Biological control strategies of mycotoxigenic fungi and associated mycotoxins in Mediterranean basin crops. *Phytopathol. Mediterr.* **2012**, *51*, 158–174.
33. Ferrigo, D.; Mondin, M.; Ladurner, E.; Fiorentini, F.; Causin, R.; Raiola, A. Effect of seed biopriming with *Trichoderma harzianum* strain INAT11 on *Fusarium* ear rot and *Gibberella* ear rot diseases. *Biol. Control* **2020**, *147*, 104826. [CrossRef]
34. Ferrigo, D.; Raiola, A.; Piccolo, E.; Scopel, C.; Causin, R. *Trichoderma harzianum* T22 induces in maize systemic resistance against *Fusarium verticillioides*. *J. Plant Pathol.* **2014**, *96*, 133–142.
35. Ferrigo, D.; Raiola, A.; Rasera, R.; Causin, R. *Trichoderma harzianum* seed treatment controls *Fusarium verticillioides* colonization and fumonisin contamination in maize under field conditions. *Crop. Prot.* **2014**, *65*, 51–56. [CrossRef]
36. Galletti, S.; Paris, R.; Cianchetta, S. Selected isolates of *Trichoderma gamsii* induce different pathways of systemic resistance in maize upon *Fusarium verticillioides* challenge. *Microbiol. Res.* **2020**, *233*, 126406. [CrossRef]
37. Adeniji, A.A.; Aremu, O.S.; Loots, D.T.; Babalola, O.O. *Pseudomonas fulva* HARBPS9.1: Candidate anti-*Fusarium* agent in South Africa. *Eur. J. Plant Pathol.* **2020**, *157*, 767–781. [CrossRef]
38. MacGee, D.C. *Maize Diseases: A Reference Source for Seed Technologists*; American Phytopathological Society Press: Saint Paul, MN, USA, 1988.
39. Bishaw, Z.; Struik, P.C.; Van Gastel, A.J.G. Farmers' seed sources and seed quality: 2. seed health. *Int. J. Plant. Prod.* **2013**, *7*, 637–658.
40. Louwaars, N. Seeds of Confusion: The Impact of Policies on Seed Systems. Ph.D. Thesis, Wageningen University, Wageningen, The Netherlands, 2007.
41. Okry, F.; Van Mele, P.; Nuijten, E.; Struik, P.C.; Mongbo, R.L. Organizational analysis of the seed sector of rice in Guinea: Stakeholders, perception and institutional linkages. *Exp. Agric.* **2011**, *47*, 137–157. [CrossRef]
42. Almekinders, C.J.M.; Louwaars, N.P. *Farmers' Seed Production: New Approaches and Practices*; Intermediate Technology: London, UK, 1999.

43. Almekinders, C.J.M.; Louwaars, N.P.; de Bruijn, G.H. Local seed systems and their importance for an improved seed supply in developing countries. *Euphytica* **1994**, *78*, 207–216. [CrossRef]
44. Almekinders, C.J.M.; Louwaars, N.P. The importance of the farmers' seed systems in a functional national seed sector. *J. New Seeds* **2002**, *4*, 15–33. [CrossRef]
45. Biemond, P.C.; Oguntade, O.; Stomph, T.J.; Kumar, P.L.; Termorshuizen, A.J.; Struik, P.C. Health of farmer-saved maize seed in north-east Nigeria. *Eur. J. Plant Pathol.* **2013**, *137*, 563–572. [CrossRef]
46. Williams, J.H.; Grubb, A.J.; Davis, J.W.; Wang, J.-S.; Jolly, E.P.; Ankrah, N.-A.; Ellis, O.W.; Afriyie-Gyawu, E.; Johnson, N.M.; Robinson, A.G.; et al. HIV and hepatocellular and esophageal carcinomas related to consumption of mycotoxin-prone foods in sub-Saharan Africa. *Am. J. Clin. Nutr.* **2010**, *92*, 154–160. [CrossRef]
47. Windham, G.L.; Williams, W.P. Comparison of different inoculating methods to evaluate the pathogenicity and virulence of *Aspergillus niger* on two maize hybrids. *Phytoparasitica* **2012**, *40*, 305–310. [CrossRef]
48. Di Giuseppe, R.; Bertuzzi, T.; Rossi, F.; Rastelli, S.; Mulazzi, A.; Capraro, J.; de Curtis, A.; Iacoviello, L.; Pietri, A. Plasma ochratoxin A levels, food consumption, and risk biomarkers of a representative sample of men and women from the Molise region in Italy. *Eur. J. Nutr.* **2012**, *51*, 851–860. [CrossRef]
49. Balasubramanian, G.; Hanumegowda, U.; Reddy, C.S. Secalonic acid D alters the nature of and inhibits the binding of the transcription factors to the phorbol 12-O-tetradecanoate-13 acetate-response element in the developing murine secondary palate. *Toxicol. Appl. Pharmacol.* **2000**, *169*, 142–150. [CrossRef] [PubMed]
50. Dhulipala, V.C.; Maddali, K.K.; Welshons, W.V.; Reddy, C.S. Secalonic acid D blocks embryonic palatal mesenchymal cell-cycle by altering the activity of CDK2 and the expression of p21 and cyclin E. *Birth Defects Res. Part. B Dev. Reprod. Toxicol.* **2005**, *74*, 233–242. [CrossRef] [PubMed]
51. Chalivendra, S.; Huang, F.; Busman, M.; Williams, W.P.; Ham, J.H. Low aflatoxin levels in *Aspergillus flavus* resistant maize are correlated with increased corn earworm damage and enhanced seed fumonisin. *Front. Plant. Sci.* **2020**, *11*, 565323. [CrossRef]
52. Landoni, M.; Puglisi, S.; Cassani, E.; Borlini, G.; Brunoldi, G.; Comaschi, C.; Pilu, P. Phlobaphenes modify pericarp thickness in maize and accumulation of the fumonisin mycotoxins. *Sci. Rep.* **2020**, *10*, 1417. [CrossRef]
53. Gao, M.; Glenn, A.E.; Gu, X.; Mitchell, T.R.; Satterlee, T.; Duke, M.V.; Scheffler, B.E.; Gold, S.E. Pyrrocidine, a molecular off switch for fumonisin biosynthesis. *PLoS Pathog.* **2020**, *16*, e1008595. [CrossRef]
54. Desjardins, A.E.; Plattner, R.D.; Lu, M.; Claflin, L.E. Distribution of fumonisins in maize ears infected with strains of *Fusarium moniliforme* that differ in fumonisin production. *Plant Dis.* **1998**, *82*, 953–958. [CrossRef]
55. Richard, E.; Heutte, N.; Sage, L.; Pottier, D.; Bouchart, V.; Lebailly, P.; Garon, D. Toxigenic fungi and mycotoxins in mature corn silage. *Food Chem. Toxicol.* **2007**, *45*, 2420–2425. [CrossRef]
56. Adejumo, T.O.; Hettwer, U.; Karlovsky, P. Occurrence of *Fusarium* species and trichothecenes in Nigerian maize. *Int. J. Food Microbiol.* **2007**, *116*, 350–357. [CrossRef]
57. Bankole, S.A.; Mabekoje, O.O. Occurrence of aflatoxins and fumonisins in preharvest maize from south-western Nigeria. *Food Addit. Contam.* **2004**, *21*, 251–255. [CrossRef] [PubMed]
58. Chilaka, C.A.; De Kock, S.; Phoku, J.Z.; Mwanza, M.; Egbuta, M.A.; Dutton, M.F. Fungal and mycotoxin contamination of South African commercial maize. *J. Food Agric. Environm.* **2012**, *10*, 296–303.
59. Soares, C.; Calado, T.; Venâncio, A. Mycotoxin production by *Aspergillus niger* aggregate isolated from harvested maize in three Portuguese regions. *Rev. Iberoam. Micol.* **2013**, *30*, 9–13. [CrossRef] [PubMed]
60. Magnoli, C.; Hallak, C.; Astoreca, A.; Ponsone, L.; Chiacchiera, S.; Dalcero, A.M. Occurrence of ochratoxin A-producing fungi in commercial corn kernels in Argentina. *Mycopathologia* **2006**, *161*, 53–58. [CrossRef] [PubMed]
61. Probst, C.; Bandyopadhyay, R.; Price, L.E.; Cotty, P.J. Identification of atoxigenic *Aspergillus flavus* isolates to reduce aflatoxin contamination of maize in Kenya. *Plant Dis.* **2011**, *95*, 212–218. [CrossRef] [PubMed]
62. Kelley, R.Y.; Williams, W.P.; Mylroie, J.E.; Boykin, D.L.; Harper, J.; Windham, G.L.; Ankala, A.; Shan, X. Identification of maize genes associated with host plant resistance or susceptibility to *Aspergillus flavus* infection and aflatoxin accumulation. *PLoS ONE* **2012**, *7*, e36892. [CrossRef]
63. Small, I.M.; Flett, B.C.; Marasas, W.F.O.; McLeod, A.; Stander, M.A.; Viljoen, A. Resistance in maize inbred lines to *Fusarium verticillioides* and fumonisin accumulation in South Africa. *Plant Dis.* **2012**, *96*, 881–888. [CrossRef]
64. Amaza, P.; Udoh, E.; Abdoulaye, T.; Kamara, A. Analysis of technical efficiency among community-based seed producers in the savannas of Borno State, Nigeria. *J. Food Agric. Environ.* **2010**, *8*, 1073–1079.
65. Daniel, I.O.; Adetumbi, J.A. Maize seed supply systems and implications for seed sector development in Southwestern Nigeria. *J. Sustain. Agric.* **2006**, *28*, 25–40. [CrossRef]
66. Saleem, M.J.; Bajwa, R.; Hannan, A.; Qaiser, T.A. Maize seed storage mycoflora in Pakistan and its chemical control. *Pak. J. Bot.* **2012**, *44*, 807–812.
67. De Curtis, F.; De Cicco, V.; Haidukowski, M.; Pascale, M.; Somma, S.; Moretti, A. Effects of agrochemical treatments on the occurrence of *Fusarium* ear rot and fumonisin contamination of maize in Southern Italy. *Field Crop. Res.* **2011**, *123*, 161–169. [CrossRef]
68. Mogensen, J.; Sørensen, S.; Sulyok, M.; Van Der Westhuizen, L.; Shephard, G.S.; Frisvad, J.; Thrane, U.; Krska, R.; Nielsen, K.F. Single-kernel analysis of fumonisins and other fungal metabolites in maize from South African subsistence farmers. *Food Addit. Contam. Part A* **2011**, *28*, 1724–1734. [CrossRef] [PubMed]

69. Chulze, S.N. Strategies to reduce mycotoxin levels in maize during storage: A review. *Food Addit. Contam. Part A Chem. Anal. Control. Expo. Risk Assess* **2010**, *27*, 651–657. [CrossRef]
70. Williams, S.B.; Baributsa, D.; Woloshuk, C. Assessing Purdue Improved Crop Storage (PICS) bags to mitigate fungal growth and aflatoxin contamination. *J. Stored Prod. Res.* **2014**, *59*, 190–196. [CrossRef]
71. Makhuvele, R.; Naidu, K.; Gbashi, S.; Thipe, V.C.; Adebo, O.A.; Njobeh, P.B. The use of plant extracts and their phytochemicals for control of toxigenic fungi and mycotoxins. *Helios* **2020**, *6*, E05291. [CrossRef]
72. Perczak, A.; Gwiazdowska, D.; Marchwińska, K.; Juś, K.; Gwiazdowski, R.; Waśkiewicz, A. Antifungal activity of selected essential oils against *Fusarium culmorum* and *F. graminearum* and their secondary metabolites in wheat seeds. *Arch. Microbiol.* **2019**, *201*, 1085–1097. [CrossRef]
73. Perczak, A.; Gwiazdowska, D.; Gwiazdowski, R.; Juś, K.; Marchwińska, K.; Waśkiewicz, A. The inhibitory potential of selected essential oils on *Fusarium* spp. growth and mycotoxins biosynthesis in maize seeds. *Pathogens* **2020**, *9*, 23. [CrossRef]
74. Loi, M.; Paciolla, C.; Logrieco, A.F.; Mulè, G. Plant bioactive compounds in pre- and postharvest management for aflatoxins reduction. *Front. Microbiol.* **2020**, *11*, 243. [CrossRef] [PubMed]
75. Veenstra, A.; Rafudeen, M.S.; Murray, S.L. *Trichoderma asperellum* isolated from African maize seed directly inhibits *Fusarium verticillioides* growth in vitro. *Eur. J. Plant. Pathol.* **2019**, *153*, 279–283. [CrossRef]
76. Lewis, M.H.; Carbone, I.; Luis, J.M.; Payne, G.A.; Bowen, K.L.; Hagan, A.K.; Kemerait, R.; Heiniger, R.; Ojiambo, P.S. Biocontrol strains differentially shift the genetic structure of indigenous soil populations of *Aspergillus flavus*. *Front. Microbiol.* **2019**, *10*, 1738. [CrossRef]
77. Gomaa, E.Z.; Abdelall, M.F.; El-Mahdy, O.M. Detoxification of Aflatoxin B1 by antifungal compounds from *Lactobacillus brevis* and *Lactobacillus paracasei*, isolated from dairy products. *Probiotics Antimicrob. Proteins* **2018**, *10*, 201–209. [CrossRef] [PubMed]
78. Abbas, H.K.; Shier, W.T.; Horn, B.W.; Weaver, M.A. Cultural methods for aflatoxin detection. *J. Toxicol. Toxin Rev.* **2004**, *23*, 295–315. [CrossRef]
79. Dimithe, G.; Debrah, S.K.; Bumb, B.L.; Gregory, D.I. *Improving Agricultural Input Supply Systems in Sub-Saharan Africa: A Review of literature*; Paper Series International Fertilizer Development Center: Muscle Shoals, AL, USA, 1998; Volume 48.