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Mycotoxins, Food and Health

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Abstract

Contamination of food and feed by fungi and the mycotoxins they produce are of common occurrence in Africa. Lifelong exposure of a large proportion of Sub-Saharan African population to foodborne mycotoxins is a reality and a serious problem. Countries in Africa lack capacity to enforce food safety regulations, and so face frequent rejection of exportable products leading to economic loss.

Improving food safety is an essential element for improving food security. A brief review is made on some issues concerning food security, namely sustainable agriculture, disruptions in the food supply chain and trade. We highlight a major agricultural threat in Sub-Saharan countries which are mycotoxins. There are different types of toxicity. These toxins are among the most potent substances known to pose acute toxicity, chronic health risks due to hepatotoxicity, immunosuppression, nephrotoxicity, estrogenic, teratogenic and/or carcinogenic effects. Prolonged exposure has been linked with liver cancer, poor nutrient absorption, retarded infant growth, malnutrition and immunosuppression.

Although the literature on mycotoxins is abundant in reports investigating cellular mechanisms, cellular toxicity, associated pathology and animal performance, studies on the effect of these compounds on general malnutrition and on the gastrointestinal tract of animals and humans is limited. The fight against mycotoxins involves the whole food chain namely the critical control points.

An innovative and promising solution of technological bio control for reducing mycotoxins is arising and under test. However, we question on the impact of this technology on biodiversity, food safety and nutrition security and enhance the need for more studies in order to evaluate its potential utilization.

Keywords: mycotoxins; regulations; biocontrol; malnutrition, food safety

Introduction

The challenge of improving food safety and security lies in involving an interdependent and interconnected set of issues, such as agriculture and fisheries, energy, setting, government policy and trade. Improving food safety is an essential element to improve food security, which exists when populations have access to sufficient and healthy food [1]. At the same time, as food trade expands throughout the world, food structure and safety has become a shared concern among developed and developing countries.

Because food safety is the result of many different actions in the food supply chain, it may be difficult to address food safety issues separately from water supply, sanitation, public health, nutrition, production and marketing issues [2]. In European Union countries, over 97% of food contain pesticide residues within legal limits while in African countries such hazards are still not seen as a major problem [3, 4].

Efforts to improve food safety in developing countries must be evaluated in terms of their impact on food security and poverty alleviation. Attempts to meet food safety standards in export markets must be judged by whether such attempts generate economic gains for the domestic industry and create positive spill overs for food safety in the domestic food system [5]. In developing countries, food safety issues will require policymakers to strengthen the capacity for evaluating the policy of trade-offs as they seek to enhance food security or to expand income generation from food trade. The global nature of the food supply will also require developed countries to consider how they might better assist developing countries to address food safety.

The Impact of Regulations on Development

Building effective regulatory structures in developing countries is not simply an issue of the technical design of the most appropriate regulatory instruments, it is also concerned with the quality of supporting regulatory institutions and capacity building.

Many new worldwide regulations involve requirements for food processing control and are based on the scientific assessment of risks and hazards that can enter the food supply chain at any one of several critical control points. Such assessments are now undertaken “from table to stable”, from “dish to fish”, from “consumer to producer” in developed countries [6].

The new regulations of the developed countries certainly have strong implications on developing country food producers and processors as these can increase costs or even block food exports [7]. During the last decade, exports of fresh and minimally processed products from developing countries, many of which are now entering in developed country markets, have increased significantly, and include mainly seafood, fish, fruits, and vegetables [8].

Developing country exporters frequently face difficulties in meeting the increasingly stringent food safety regulations imposed by developed countries [9]. Technical assistance, investments by producers, and new policies in developing countries, however, have all played a role in helping developing country exporters maintain market access, albeit the lack of coherence observed in some African governmental decisions, namely on control of Genetically Modified (GM) crops [10, 11].

The food system is also changing in developing countries themselves, not least because new food safety standards, required by the developed world, are shaping expectations among most urbanized consumers [12]. Moreover, processing and preparation of food ceases to be a familiar process to become an industrialized one, as economies develop and rapid modernization happens in the food sector in developing countries, where consumers are becoming increasingly more demanding with regard to food security. As the food system changes, many kinds of hazard-mitigation activities are also shifting from the households to the food industry, and it is not always clear who bears responsibility for food safety or its cost [13].

Regulations throughout the world do not consider the combined effects of mycotoxins. However, several surveys have reported the natural co-occurrence of mycotoxins from all over the world. Most of the published data concerns the major mycotoxins aflatoxins, fumonisins, ochratoxin A, zearalenone, citrinin, ergot alkaloids, patulin, trichothecenes, and deoxynivalenol (DON). It is necessary that food safety, in spite of the coexistence with informal food markets, is regarded as an essential component of health-based nutrition policies and nutrition education, both still in their early stages of development in Sub-Saharan Africa.

Mycotoxins in the food chain

Most fungi, and mushrooms are fungi, do not produce mycotoxins. Thousands of mycotoxins exist, but only a few present significant food safety challenges. They are secondary metabolites of fungi and are associated with certain disorders in animals and human beings. Mainly produced by species from the *Aspergillus, Penicillium*, and *Fusarium* genera which can develop during production, harvesting, or storage of grains, nuts, tubers and other crops [14]. Mycotoxins are among the most potent mutagenic and carcinogenic substances known. They pose chronic health risks: prolonged exposure through diet has been linked to cancer and kidney, liver, and immune system diseases [15].

These toxins are found all around the world as natural contaminants in numerous commodities of plant origin, especially in cereals grains, but also in nuts, oilseeds, fruits, dried fruits, vegetables, cocoa and coffee beans, wine, beer, as well as herbs and spices. Unlike bacterial toxins, fungal mycotoxins are not proteins and therefore are not usually detectable by the immune systems of humans and animals.

In Mozambique there is a commercial beer made from fresh cassava but levels of these toxins were never evaluated. Mycotoxins can also be found in animal-derived food if animals eat contaminated feed, namely meat, eggs, milk, and milk derivatives [16, 17].

Some foods and feeds are often contaminated by numerous mycotoxins but most studies have focused on the occurrence and toxicology of a single mycotoxin (Figure 1). Toxins can remain in the organism after the fungus has been removed.

Figure 1: Maize corn contaminated by mould and aflatoxin.

Mycotoxin ingestion may induce various chronic and acute effects on humans and animals, such as hepatotoxic, genotoxic, immunosuppressive, estrogenic, nephrotoxic, teratogenic, and/or carcinogenic effects [18]. Moreover, mycotoxins are not completely eliminated during food processing operations and can contaminate finished processed food products [19, 20].

In contrast to the infectious diseases, mycotoxins, because of their chronic effects on human being, have been neglected in most developing countries. No data is available on mycotoxin contamination of Mozambican commodities although our own unpublished surveys, conducted on samples from a cooperative with some 120,000 small producers, showed levels of contamination of 100% of dried "grey" cassava (a staple food in the northern region) (Figures 2, 3).

Many countries have regulations specifying the maximum allowed concentration of mycotoxins, but there are no regulations requiring measures to reduce contamination. If not legally required, producers are reluctant to invest in approaches that would reduce mould growth. Considerable effort, however, is spent on quantifying mycotoxins in food and on developing

Figure 2: Cassava contaminated by mould and mycotoxins.

Figure 3: Cassava drying on roofs.

methods that are able to detect increasingly lower concentrations. Perhaps now is the time to divert some of these efforts towards methods that reduce the problem, specifically preventing mould growth and affordable methods to eliminate mycotoxins from contaminated food. These also require education and training of those who need to apply the knowledge.

The occurrence of mycotoxins in the food chain is well known (Figure 4). While deleterious effects of feed mycotoxin contaminants in animals and humans are well documented, data with regard to their impact on intestinal functions are more limited. However, intestinal cells and the microbioma are the first cells to be exposed to mycotoxins, and often at higher concentrations than other tissues. In addition, mycotoxins specifically target high protein turnover- and activated-cells, which are predominant in gut epithelium.

Therefore, intestinal investigations have gained significant interest over the last decade, and some publications have demonstrated that mycotoxins are able to compromise several key functions of the gastrointestinal tract, including decreased surface area available for nutrient absorption, modulation of nutrient transporters, or loss of barrier function. In addition some mycotoxins facilitate persistence of intestinal pathogens and potentiate intestinal inflammation. By contrast, the effect of these fungal metabolites on the intestinal microbioma is largely unknown [21].

The chemical structures of mycotoxins produced by these fungi are very diverse as are the characteristics of the mycotoxicoses they can cause (Figure 5) [22].

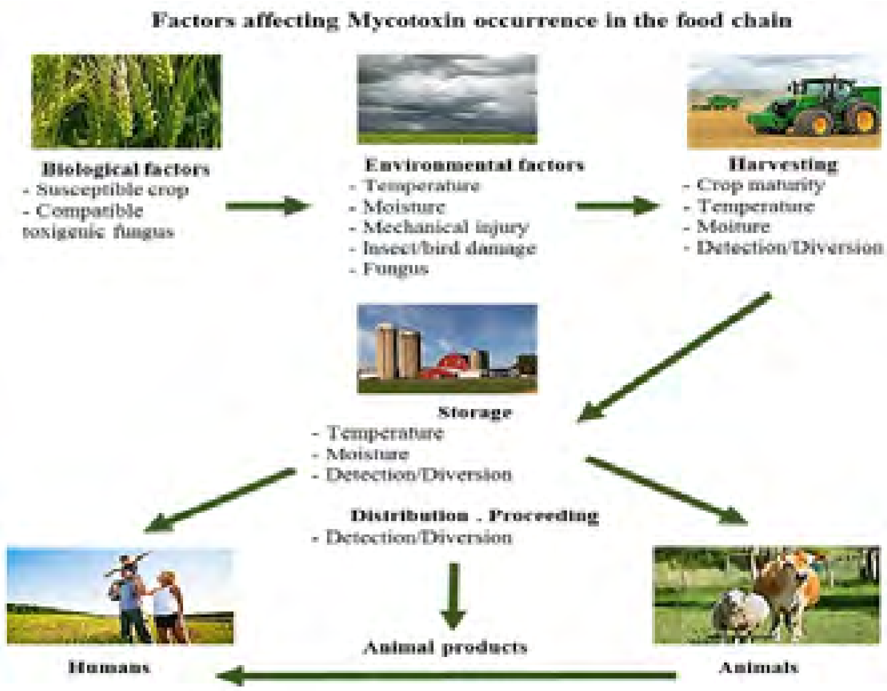

Figure 4: Factors affecting mycotoxin occurrence in the food and feed chain.

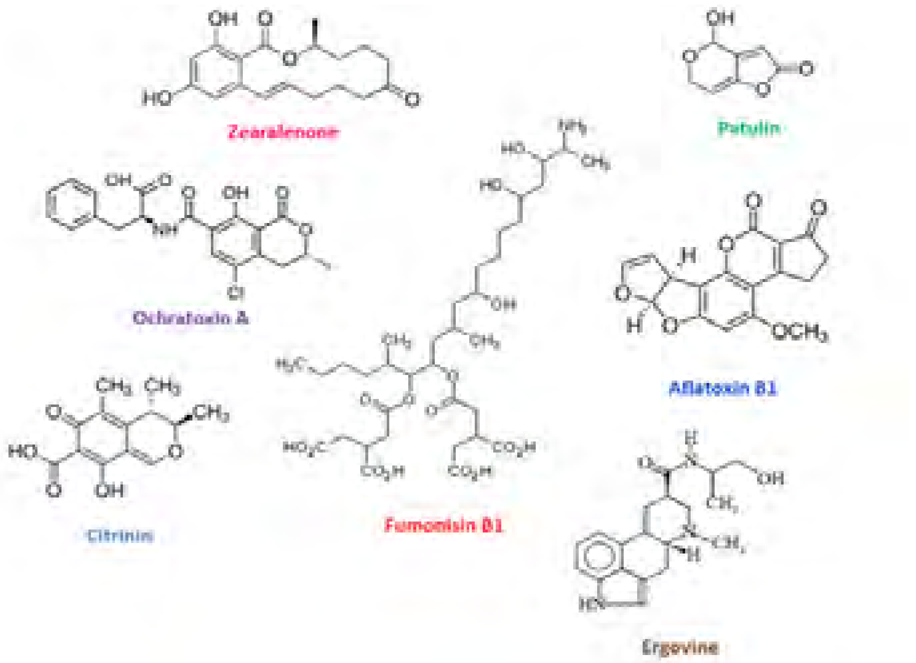

Figure 5: The chemical structure of some mycotoxins.

Because of their pharmacological activity, some mycotoxins or mycotoxin derivatives have found use as antibiotics, growth promoters, and other kinds of drugs; still others have been implicated as chemical warfare agents. The most important ones are associated with human and veterinary diseases induced by oxidative stress producing free radicals. Oxidative stress plays a major part in the development of chronic and degenerative illness (Figure 6). The human body has several mechanisms to counteract oxidative stress by producing antioxidants, which are either naturally produced *in situ*, or externally supplied through foods and/or supplements [23].

The levels in local foodstuffs of the first four mycotoxins are being investigated in the Mozambican laboratory at CEIL, Lúrio University in Nampula for the purpose of allowing exports of local produce namely peanuts (Figure 7).

Quantitation of mycotoxins in food and feed from Burkina Faso and Mozambique using a modern LC-MS/MS multitoxin method was conducted emphasizing the great variety of mycotoxin co-exposure [24].

Because mycotoxins occur more frequently under tropical conditions, crops of many developing countries, where diets are heavily concentrated in those cultures, are more susceptible to develop mycotoxins [25]. Additionally, mycotoxins can also be present in livestock feed, reducing meat and dairy production (Figure 8) [26]. If these toxins find their way from feed into milk or meat, they might become a food safety hazard of these products too. In food manufacturing, destruction of mycotoxins by conventional food processing is difficult because they are typically highly resistant and detection is complicated due to limitations in analytical methodology.

Human exposure to levels of aflatoxins from nanograms to micrograms per day occurs through consumption of maize, cassava and peanuts which are dietary staples in several tropical countries (Table 1) [27]. The chronic incidence of aflatoxin in diets is evident from the presence of aflatoxin in human breast milk [28]. Some authors demonstrate the role of aflatoxicosis in general chronic malnutrition [29]. Others state that increasing levels of aflatoxins are linked to an increased prevalence of stunting and underweight [30]. Very little is known about the effects of long-term low-level exposure, especially with regard to co-contamination with multiple mycotoxins. Also, due to the heterogeneity of mycotoxin contamination and the potential for sampling regions with elevated toxin levels ("hot spots"), consistent sampling and analysis is difficult [31]. Thus, development of low-tech, inexpensive methods for mycotoxin surveillance is a world health imperative. With several novel approaches being developed, such as molecular imprint polymers and immune- and bio-assays [32, 33].

Food quality along the chain from production through marketing to consumption must remain a key element in the nutrition agenda. It is possible, based on existing suggestive evidence that reducing the burden of aflatoxin contamination in the food supply may contribute significantly to the overall reduction in child stunting [34].

Figure 6: Oxidative stress-induced diseases in humans.

Figure 7: Aflatoxin-contaminated groundnut kernels from Mozambique (credit IITA).

Figure 8: Feeds and Foods that may be contaminated.

In parts of the world where food supply is limited, drastic regulatory measures to lower mycotoxin standards would lead to food shortages and to higher prices. The observation made during the outbreak of aflatoxin hepatitis in western India in 1974 that "starving to death today by not consuming contaminated food in order to live a better life tomorrow is not a practical option" is relevant even after 40 years [35]. Thus, any preventive measures must be pro-poor, well focused, and cost-effective.

A focus on high-risk agricultural commodities, during high-risk seasons in high-risk areas and among high-risk population groups, for selected mycotoxins would yield great public health benefits. Monitoring human population groups for diseases attributable to mycotoxins, coupled with the implementation of appropriate prevention and control measures, including decontamination and detoxification, would ensure a food supply free from mycotoxins [36]. In the long term, such investments would be offset by better human and animal health and reduced economic losses.

Modified mycotoxins (often called "masked" or "bound forms") are metabolites of the parent mycotoxin formed in the plant or fungus, e.g. by conjugation with polar compounds. For instance, fumonisins, which are difficult to extract from the plant matrix, are also termed as modified mycotoxins [37]. Therefore, it is appropriate to assess human exposure to modified forms of the various toxins in addition to the parent compounds, because many modified forms are hydrolysed into the parent compounds or released from the matrix during digestion [38].

The objective of controlling mycotoxin levels in foodstuffs is to improve income and health of farm families and generate wealth in the crop value chain. Developing and making available, commercially ready cost-effective biological control technology for aflatoxins, in combination with other practices, will improve public health, increase the agricultural trade, augment smallholder income, and enhance food security.

In developing countries, monitoring and enforcement of standards is rare. Regional and international experts in agriculture, health, research and trade have drawn up a plan of action for the control of aflatoxins in Africa pointing some five priority strategic thematic areas have been identified for action: 1) Research and technology for control of aflatoxins; 2) Legislation, policies and standards in the management of aflatoxin in Africa; 3) Growing commerce and trade while protecting lives from aflatoxins; 4) Enhancing capacity building on aflatoxin management, control and regulatory processes to ensure reduced exposure; and 5) Public awareness, advocacy and communication [39].

Table 1: Example of maximum tolerance limits, variable with countries. (T2= trichothecene); (DON=Deoxynivalenol)

	Maximum tolerance limit
Aflatoxin	20 ppb
Ocharatoxin	40 ppb
Citrinin toxin	100 ppb
Zearalenone	400 ppb
DON (Vomitoxin)	5 ppb
T2 toxin	200 ppb

Detecting Mycotoxins in Human Breast Milk

Human milk is an ideal and most bio-available source of calcium and protein for infants. It also contains suitable amounts of carbohydrate and fat. The first studies on mycotoxin occurrence in human milk date back to the mid and late 80's and examined the presence of aflatoxins and ochratoxin A in breast milk samples collected in Germany and in some countries of tropical Western Africa [40]. Since then, many more studies have been conducted in other parts of the world. The reported frequencies of detection and average concentrations of aflatoxins (B1, M1) indicate that exposure of infants in Europe is low or negligible, but can reach critical levels in Tropical Africa and some countries of the 'Middle East'.

Mycotoxins that offer higher risks to child health are aflatoxins B1, M1 and ochratoxin A, commonly present in foods consumed by children, such as milk and dairy products. Even breast milk can be a vehicle for the transfer of mycotoxins to babies, since the mycotoxins contained in food ingested by the mother may pass into her milk, continuing childhood exposure to these compounds, initiated in utero [41]. Children's exposure to mycotoxins (and various other toxic compounds) may start immediately after conception, as many contaminants cross the placenta, and continues throughout life, entering the human body through food, water and air [42].

Few studies indicate that there is contamination of mycotoxins (over 60%) from lactating women and breast feeding infants. The toxin levels are alarmingly high, and indicate that Sudanese infants are exposed to high level of aflatoxins M1 and even a study in Spain the contamination levels were very high [43, 44]. The ideal process for the evaluation of mycotoxin exposure in human populations is the measurement of biomarkers in bodily fluids. Breast milk, in particular, may reveal both maternal and neonatal exposure levels. Unfortunately, the data currently available for mycotoxin levels in human breast milk are limited.

In Germany, studies were conducted with human milk contaminated with ochratoxin A and levels of average 50% contaminated were found. The infants' exposure was assessed by calculating their ochratoxin A intake via human milk [45]. This demonstrates the need to conduct specific studies in each country to determine levels of contamination of different commodities.

Biological control of aflatoxins in Africa

In a non-published study of ours, at the University Eduardo Mondlane, Maputo, in 2004, we looked at the effectiveness of Mozambican Diatomaceous Earth (DE) and Bentonite Clay (BC) in reducing the toxic effects of aflatoxin B1 in chicks. Although deposits of DE and BC are available in Mozambique their potential as a feed additive mycotoxin binder was not assessed previously. DE was not effective in reducing toxic effects while BC showed promising data but both trials needed replication. Further research from an extended international research group confirmed those previous results [46].

Food quality and safety issues resulting from aflatoxin contamination present a serious obstacle to programmes designed to improve nutrition and agricultural production that link small farmers to markets. Aflatoxin control strategies can be enormously cost-effective from a health–economic standpoint in countries where these are most needed. While it is impossible to completely eliminate aflatoxins on food worldwide, it is possible to reduce levels significantly and thus dramatically reduce the known adverse effects [47].

Some mycotoxins levels have been shown to be reduced in the field and in storage without intervention, as discussed by Karlovsky [48]. Some research efforts are focusing on methods to prevent infection at the pre-harvest stage with emphasis on mechanisms by which the affected plants may inhibit growth of moulds or destroy mycotoxins that they produce. There has been limited success with this approach. There are hybrids currently in use that limit mycotoxins production; however, the potential to reach acceptable levels remains. Genetic modification of mould-susceptible plants holds great promise for controlling this food safety issue [49].

The potential for using microorganisms to detoxify mycotoxins has shown promise. Exposure to microbes contained in the contents of the large intestines of chickens and ruminants completely detoxified the mycotoxins [50, 51].

Symbiosis between plants and microbes is extensive in nature and used in agriculture. How such genetic interactions work requires more research. Symbiotic microbes can be added to seed as treatment or applied to the roots where they invade the plant to establish a mutually beneficial relationship with plant cells. Most plants get their mineral nutrients from a partnership with a fungus and research is going on gene exchanges between plant and fungus providing insights into ways that plant cells host their fungal symbionts. This technology aimed at boosting crop yield and reduced fertilizer use.

In this line of work an innovative biocontrol solution was developed by IITA to reduce the aflatoxin contamination [52]. This breakthrough technology, already widely used in the United States, reduces aflatoxins during both, crop development and postharvest storage, as throughout the value chain. Atoxigenic strain-based biological control is a natural, nontoxic technology that uses the ability of native atoxigenic strains of *Aspergillus flavus* (the fungus that produces aflatoxin) to naturally outcompete their relatives, aflatoxin producers.

This North American technology, trade mark registered as "Aflasafe"®, successfully adapted to be used in Africa (Nigeria, Senegal, Burkina Faso, Kenya, Gambia) and currently being developed for Mozambique, Zambia, Tanzania, Rwanda and Ghana, uses a native micro-flora, and has developed a registered as a biocontrol product. Field-testing over the past 6 years in Nigeria has produced extremely positive results: the aflatoxin contamination in maize and groundnut was consistently reduced by 80–90% and in some cases even by 99% [53].

Native atoxigenic strains have been isolated in Kenya, and are ready for further evaluation in order to become a product. This technology, currently being tested in Mozambique, is considered particularly effective in the African context because it addresses the source of aflatoxin—the fungus in the soil—before it can contaminate the crop, prior to the harvest. Adapting and applying this solution to address aflatoxin contamination in Africa, could dramatically improve the health and livelihoods of millions of families while reducing commodity losses due to contamination. The application of registered trade mark technologies does not increase the total amount of *Aspergillus* in the environment, but shifts the profile from toxigenic to atoxigenic strains. A single application is effective for several, maintaining this efficacy since the field until store and thus, protecting maize/groundnut along the entire value chain (from field to fork) [54].

This project aims to verify the efficacy and enable the commercialization of the biocontrol product and the identification of biocontrol strains for registration in each country. Adoption of this biocontrol technology with other management practices by farmers may reduce aflatoxin contamination by >70% in maize and peanut, increase crop value by at least 5%, and improve the health of children and women [55].

Many countries do not have the resources to effectively monitor foodstuffs neither intervenes if necessary at the local level. Even if the resources were made available, it is widely agreed that a reliance on formal testing and lot destruction is both inefficient and ineffective as a way to the control of food contaminants [56]. This is because testing for mycotoxins is challenging due to the heterogeneous distribution of mould growth. Collecting the required sample is generally time-consuming and costly. As such, it has been argued that the adoption of best practices at every step in the food chain needed to minimize mould infection, prevent its spread, and reduce the levels of toxins in the diet, requires clear Codes of Practice to be developed by national governments [57].

The Impact of New Technologies on Biodiversity and Food Security

Biotechnology alone will not bridge the food gap in Africa. Because agriculture accounts for some 16% of African gross domestic product improvements in infrastructures are crucial to the continent's development [58]. The application of science and technology into agriculture requires extensive coordination across many actors and sectors including political leadership [59].

The African Union recently adopted a new 10-year vision of science, technology and innovation—including hunger eradication and ensuring food and nutrition security as one of the six designated pillars [60]. Although most African nations had looked to biotechnology cautiously, it is believed that educating countries about new technologies is important as more evidence becomes available about the technology's safety and potential benefits. The growing public opposition to innovative technologies in Africa is best described as a fear of the unknown.

Developing countries' resulting dependency on western biotechnology companies may grow and threaten local farmers, especially smaller ones. Moreover, some claim that new technologies are leading to a reduction in biodiversity [61]. More and more monoculture crops (like soya or maize) are being harvested for export and not for primarily domestic consumption, like staple/sustenance crops (e.g. maize or cassava) [62]. This trend may lead to a dependency of multinational biotechnology companies and endanger the existence of smaller farmers.

Without an accompanying social security system, poor harvests may have dramatic consequences on local farmers. At a more fundamental level, only a resilient and sustainable agriculture that is based on a wide variety of crops can assure a country's food security. Therefore, it is still not clear if the current support for new technologies such as the bio control technique described above may endanger traditional crops as well as biodiversity as a whole [63, 64]. Furthermore, the relationship between treated crops with products such as native atoxigenic strains and the biodiversity, taking into account the agro-ecology as a potentially beneficial concept for smallholders in developing countries, still needs to be evaluated.

There is a need for a comprehensive study focusing on long-term effects of new technologies on the environment and health, identifying potential different environmental risks [65]. Although it is not yet possible to quantify long term risks of adoption of new technologies because "experience is lacking", questions may arise over potential future environmental risks such as potential impacts on soil and on soil organisms with a high degree of uncertainty due to a limited number of studies available.

While there is still insufficient evidence for clear conclusions, and knowing that regional differences have to be taken into account, some of these risks have meanwhile become a harsh reality in certain regions [66].

Concluding Remarks

Food safety is a major concern in most African countries due to the lack of knowledge, education and sanitation, which are key to improvements in public health and nutrition security. Studies measuring levels of mycotoxins in foods, feeds and breast milk have been scarce.

The potential impact of aflatoxins in diets and in nutritional status is bi-directional: if on one hand there are actions aimed at protecting the food supply for being potential targets of aflatoxin growth, on the other hand must be actions aimed at enhancing the natural immunity of consumers, meaning preventing malnutrition.

In the future, much attention should be paid to low concentrations of mycotoxins, even though moderate doses can be encountered occasionally during unfavourable weather conditions. Global attention must focus on the potential role played by mycotoxins in the quality of food, as it is a cause of several illnesses, child malnutrition and impaired growth, and of reproductive outcomes in animals.

Adopting new technology of aflatoxin control may address a serious food safety issue and the benefits will be extended to the entire value chain: from small producers and their families who eat their own production, to food and feed processors, until final food consumers, especially groups with increased vulnerability to diseases, particularly women. However, there is a need of long term ecology studies of these new technologies and evaluation of the risk management trade-offs in terms of tolerable levels of mycotoxins in humans.

The available, updated information on the incidence of mycotoxin contamination, decontamination and its public health importance in Africa is lacking. This may be due to limited monitoring systems and failure to adopt preventive and control measures in these countries.

The question is whether the dependence of a registered technology may or may not surpass the necessary adoption of best practices, at every step in the food chain, needed to minimize undernourishment, mould infection and prevent its spread, and reduce toxin levels in the diet, requiring clear Codes of Practice to be developed by national governments in developing countries.

Africa will benefit from a more fruitful, peer-to-peer exchange with North American and European developed country counterparts, learning with them how to minimize mould contaminations and ultimately helping farmers to improve their livelihoods. However, cannot be dependent for good on new technologies and must create its own methodologies and structures for mycotoxin control of its own commodities.

In a future where climate change may significantly affect the worldwide distribution and contamination by mycotoxigenic fungi and mycotoxins, the analysis of levels of contamination as well as the implementation of prevention and control strategies will be of major concern.

Authors' Contributions

All authors contributed to the conceptualization and to the writing of the manuscript and declare no conflict of interests.

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