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Review

Predicted Aflatoxin B_1 Increase in Europe Due to Climate Change: Actions and Reactions at Global Level

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Abstract: Climate change (CC) is predicted to increase the risk of aflatoxin (AF) contamination in maize, as highlighted by a project supported by EFSA in 2009. We performed a comprehensive literature search using the Scopus search engine to extract peer-reviewed studies citing this study. A total of 224 papers were identified after step *I* filtering (187 + 37), while step *II* filtering identified 25 of these papers for quantitative analysis. The unselected papers (199) were categorized as "actions" because they provided a sounding board for the expected impact of CC on AFB_1 contamination, without adding new data on the topic. The remaining papers were considered as "reactions" of the scientific community because they went a step further in their data and ideas. Interesting statements taken from the "reactions" could be summarized with the following keywords: Chain and multi-actor approach, intersectoral and multidisciplinary, resilience, human and animal health, and global vision. In addition, fields meriting increased research efforts were summarized as the improvement of predictive modeling; extension to different crops and geographic areas; and the impact of CC on fungi and mycotoxin co-occurrence, both in crops and their value chains, up to consumers.

Keywords: *Aspergillus flavus*; mycotoxin; crop modeling; predictive model; co-occurrence; food; feed; risk assessment; safety

Key Contribution: Advances in modeling the impact of climate change (CC) on aflatoxin occurrence in maize over the last decade have been limited, mainly being considered by Italy, the United Kingdom and the United States, with few contributions from the continents where mycotoxin contamination is a major problem (Africa and Asia). Interestingly, related topics have been purposed, such as the co-occurrence of fungi and their impact on mycotoxin contamination, the chain approach (from cropping season to final products of the value chain), and the link between the expected increase in aflatoxin occurrence resulting from CC and its impact on human and animal health.

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1. Conceptual Framework

The mycotoxins of greatest concern to food and feed safety are produced by members of a few genera of filamentous fungi, with *Aspergillus*, *Fusarium* and *Penicillium* playing a key role. These fungi colonize many crops and are adapted to a wide range of environmental conditions, having different but partially overlapping ecological niches [1]. A key point of interest in relation to maize are the aflatoxin (AF) producers *Aspergillus flavus* and *A. parasiticus*, *Fusarium verticillioides* and *F. proliferatum*, known for fumonisin (FB) production, and *F. graminearum*, able to biosynthesize both trichothecenes, such as deoxynivalenol (DON), and zearalenones (ZEN) [2,3]. Among staple crops, maize is of concern for mycotoxin contamination; mycotoxins are regulated in Europe and in several other countries worldwide, and several co-occurring fungal organisms are often detected [4].

Knowledge of environmental factors affecting fungal survival, growth, metabolic activity and interaction with other organisms, including host plants, is essential for understanding their dynamics and the resulting toxin contamination [5]. The environment provides all the leading factors for mycotoxin prevalence. In particular, high temperatures and drought stress directly affect maize and the occurrence of *A. flavus*, favoring fungal growth, conidiation and spore dispersal, and impairing the growth and development of maize [6]. FB-producing fungi can be found wherever maize is grown, but their occurrence varies geographically. FB occurrence is typically higher in maize-growing areas at low latitudes and elevations, where conditions are relatively warmer compared with those of high-latitude or high-altitude maize-growing regions where [7–9], on the contrary, DON is commonly dominant [2].

Climate change (CC) is predicted to have a significant impact on the security of staple commodities. Based on available data, atmospheric concentrations of CO_2 are expected to double or triple (from 350–400 to 800–1200 ppb) in the next 25–50 years. Therefore, different regions of Europe is expected to face increases in temperature of 2–5 °C coupled with elevated CO_2 (800–1200 ppm) and drought episodes, with concomitant effects on pests and diseases and ultimately crop yield [10–12], as well as mycotoxins. Until a few years ago, AFs had not been identified as a matter of concern for primary production in Europe. However, the year 2003 saw the first alarming contamination of maize in Italy [13]. AFs are potent carcinogens existing as four primary structural analogues: AFB_1, AFB_2, AFG_1 and AFG_2. The International Agency for Research on Cancer (IARC) has classified AFB_1 as a Group 1A carcinogen, i.e., carcinogenic to humans [14]. In addition to hepatocellular carcinoma, AFs are associated with occasional outbreaks of acute aflatoxicoses, leading to death shortly after exposure [15].

The European Food Safety Authority (EFSA), with a mandate to identify emerging risks in the food and feed sectors, has identified changing patterns in mycotoxin production in cereals due to CC as a potential matter of concern. Therefore, in 2009, the EFSA's Emerging Risks Unit delivered a call for scientific information (CFP/EFSA/EMRISK/2009/01), based on models and scenarios, to predict the possible increase of AFs in cereals in the EU due to CC. Two CC scenarios, +2 °C and +5 °C above pre-industrial levels, which consider whether or not mitigation strategies for CC are applied, in addition to the present (baseline) scenario were considered in the funded project, MODMAP-AFLA. These scenarios provided the data input for AFLA-maize [16], a mechanistic model, able to predict AF contamination risk using weather data as input. The project's output predicted an increased risk of AF contamination in maize in the future [17,18]. Findings also suggested that CC effects will be (*a*) regional; and (*b*) detrimental or advantageous depending on geographical region and the CC scenario considered [18]. In northern Europe, the effects may be positive, with the enlargement of maize growing area without or with minimal AF risk. Conversely, the Mediterranean basin is expected to be a hot spot of many adverse effects, with extreme changes in rainfall/drought, elevated temperatures and CO_2 impacting food production and AF contamination in maize.

In this study, we identified the actions and reactions of the scientific community based on the results of the MODMAP-AFLA project [17,18].

1.1. Dataset Creation: Scientific Paper Search, Filtering, and Selection

A comprehensive literature search was performed using the Scopus search engine to extract peer-reviewed studies that were published until the end of 2020 (Scopus last access 28 March 2021). The citations included, either (*a*) the EFSA report: Modelling, predicting and mapping the emergence of aflatoxins in cereals in the EU due to climate change [17]; or (*b*) the accompanying manuscript: AFB_1 contamination in maize in Europe increases due to CC [18].

Two-step filtering was conducted during database creation. The step *I* exploited the exclusion criteria available directly in the Scopus search engine: Document type, and language (Figure 1). Only papers, conference papers, and book chapters published in English were selected.

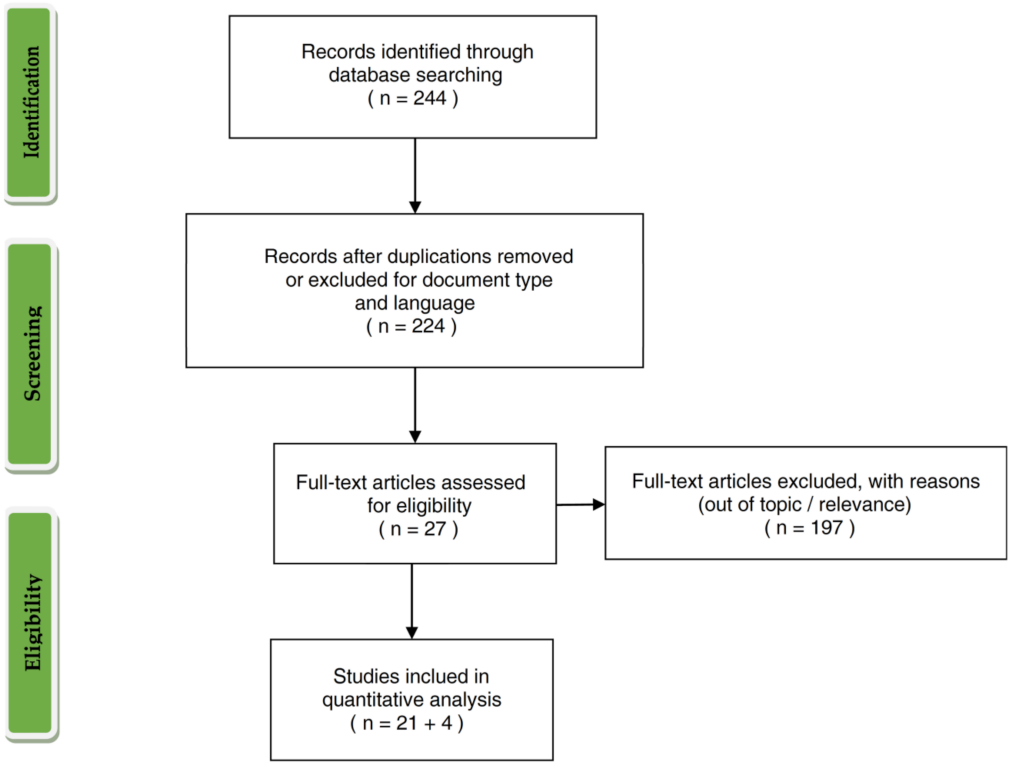

Figure 1. Workflow showing the phases of paper selection.

Bibliometric metadata for the selected research papers were then exported from the Scopus search engine. Metadata text files were elaborated using the scientific mapping software VOSviewer [19].

1.2. Topic Categorization and Other Classification Criteria

A second level of filtering was performed to determine eligibility of the selected research papers, based on the following exclusion criteria: (*a*) Adequacy of the paper topic to match the objectives of aflatoxin and CC; (*b*) mixed criterion accounting for at least one topic within (*a*) crop model, (*b*) fungal model, (*c*) weather data, (*d*) climate data, (*e*) current impact, (*f*) future impact and (*g*) single occurrence or co-occurrence (Table 1). For all papers compliant with at least one of the aforementioned criteria, the authors extracted information about the area of study and matrix. The authors then proceeded with a careful reading of the full text of each eligible article.

2. Motivations Underpinning Action-Reaction Analysis

This review considers all papers citing the output of EFSA project MODMAP-AFLA [17] on the effect of CC on *A. flavus* and AF contamination in maize across Europe [18].

Step *I* filtering identified 224 papers [5,6,20–242]: 187 citing Battilani, et al. [18] and 37 citing Battilani, et al. [17]. Step *II* filtering identified 25 papers (Table 1; 21 citing [18] and 4 citing [17]) relevant to the study, which were included in a deeper analysis. These papers were categorized as "*reactions*" to the cited results because they went a step further. All the other papers (199) were considered "*actions*" following those publications; they played the role of sounding board for the expected impact of CC on AFB_1 contamination, without adding new data on the topic.

The overall workflow of database creation with single steps and corresponding number of selected or excluded papers is shown in Figure 1.

Table 1. Overall research paper dataset tabulated according to topic categorization. Reference number refers to bibliography reference; Study area as ISO 3166-1 alpha-2 country code, otherwise Continents or Global for larger study area; a_w = water activity; AFB_1 = aflatoxin B_1; WOFOST = WOrld FOod STudies; DON = deoxynivalenol; JRC MARS = Joint Research Centre Monitoring Agricultural ResourceS; DAYMET = daily weather observation data; CRONOS = Climate Retrieval and Observations Network Of the Southeast; ECHAM5 = Global climate model 5th generation; HadCM3Q0 = Hadley Centre Coupled Model version 3, A1B Special Report on Emissions Scenarios; HadGEM2-ES = Hadley Centre Global Environment Model version 2 Earth System; RACMO2 = Regional Atmospheric Climate Model version 2; HADRM3Q0 = Hadley Center Regional Model version 3, A1B Special Report on Emissions Scenarios; AFM_1 = aflatoxin M_1; OTA = ochratoxin A; AFs = aflatoxins; FBs = fumonisins; NIV = nivalenol; ZEN = zearalenone.

Reference	Study Area	Matrix	Model Approach	Weather Data	Climate Scenario	Current Impact	Future Impact	Mycotoxin Occurrence	Co-Occurrence
Djekic, et al. [64]	RS	Milk and dairy products	NO	Speculative	Speculative	2015–2018	NO	AFM1 (AFB_1 in feed)	NO
Hiatt and Beyeler [94]	Global	Speculative	Speculative	Speculative	Speculative	Speculative	Speculative	General	NO
Adhikari, et al. [21]	Global	Coffee	Speculative	Speculative	Speculative	Speculative	Speculative	OTA-AFs-FBs	NO
Fouché, et al. [78]	Global	Soil/Food/Feed	Speculative	Speculative	Speculative	Speculative	Speculative	AFs	NO
Cervini, et al. [47]	IT *	Grape	Water/light/temperature in lab conditions	LAB conditions	Speculative	Speculative	Speculative	OTA	NO
Camardo Leggieri, et al. [45]	IT	Maize	aridity index-correlation index	Air temperature, rainfall, relative humidity	Speculative	2014	Speculative	NIV-DON-T2-HT2-ZEN-FBs-AFB1	YES
Pleadin, et al. [151]	Europe	Food/Feed	Speculative	Speculative	Speculative	Speculative	Speculative	AFB_1-OTA-FBs-PATULINE-DON	NO
Gasperini, et al. [85]	BR/MX **	Maize	Pre/post harvest + interactions of Air temperature × CO_2 × a_w	LAB conditions	Speculative	Speculative	Speculative	AFB_1	NO
Van der Fels-Klerx, et al. [191]	NL/UA	Maize feed in UA/Milk in NL	3 climate models + AFB1 model + WOFOST+ 5 carryover models	JRC MARS	ECHAM5, HadCM3Q0	2005–2017	2030	AFB_1-AFM1	NO
Moretti, et al. [131]	Europe	Food	Speculative	Speculative	Speculative	Speculative	Speculative	AFs-DON	NO
Labanca, et al. [118]	IT	Maize for feed	Speculative	Speculative	Speculative	Speculative	Speculative	AFs	NO
Ricciardi, et al. [159]	Global	Food	Speculative	Speculative	Speculative	Speculative	Speculative	General	NO
Cervini, et al. [48]	IT	Grape	NO	LAB conditions	NO	Speculative	Speculative	OTA	NO
Iizumi [99]	Global	Speculative	Speculative	Speculative	Speculative	Speculative	Speculative	General	NO
Bailly, et al. [31]	FR	Maize	Speculative	Speculative	Speculative	Speculative	Speculative	AFB_1	NO
Damianidis, et al. [57]	US	Maize	Logistic regression	Weather stations, DAYMET, CRONOS	NO	Speculative	Speculative	AFs	NO
Fanzo, et al. [72]	US	Food/ Feed	Speculative	Speculative	Speculative	Speculative	Speculative	General	NO
Assunção, et al. [30]	PT	Dietary exposure	NO	Speculative	Speculative	Speculative	Speculative	AFs	NO
Medina, et al. [128]	GB	Food	Speculative	Speculative	Speculative	Speculative	Speculative	General	YES
Raiten and Aimone [157]	CA/US	Speculative	Speculative	Speculative	Speculative	Speculative	Speculative	General	NO
Magan and Medina [121]	GB	Maize and Coffee	Linear regression	Lab conditions	Speculative	Speculative	Speculative	All mycotoxins	NO
Van de Perre, et al. [241]	ES/PL	Tomato	Climate + Alternaria model	Weather stations	HadGEM2-ES	1981–2000	2031–2050 2081–2100	Alternaria	NO
Giorni, et al. [211]	GB/IT	Maize	NO	NO	NO	NO	NO	AFs	NO
Van der Fels-Klerx, et al. [242]	Europe ***	Wheat	Wheat phenology + Climate + DON model	JRC MARS	RACMO2, HADRM3Q0	1975–1994	2031–2050	DON	NO
Medina, et al. [226]	Global	Feed/Food	Data from review + in vitro data	Speculative	Speculative	Speculative	Speculative	All mycotoxins	NO

* Lab/in vitro study reproducing climatic conditions of Apulia region (Italy); ** combination of in situ and in vitro studies; *** refers to north-western Europe.

3. Overview of Selected Papers

The results of the scientific mapping, including papers categorized as "*actions*" and "*reactions*," are summarized in four figures highlighting the journal where papers were published, keywords and their link to each other, and the countries to which the authors were affiliated (Figures 2–5).

The source titles for all research papers filtered through the exclusion criteria during the screening process (step *I*—224 papers) are shown in Figure 2. *Toxins* (MDPI) turned out to be, by far, the most popular journal for publication, accounting for 14.3% (32 papers) of the filtered publications, followed by *World Mycotoxin Journal* (9.8%, 22 papers—Wageningen Academic Publishers), *Frontiers in Microbiology* (4.5%. 10 papers—Frontiers Media), *Food Additives and Contaminants—Part A Chemistry, Analysis, Control, Exposure and Risk Assessment* (3.6%, 8 papers—Taylor & Francis Online) and *Microorganism* (2.7%, 6 papers—MDPI).

Despite most of the selected articles (89%, 199 papers) citing Battilani, et al. [17] and Battilani, et al. [18] only in the introduction, or not providing substantial advances to the topic covered by these two publications, our keywords occurrence analysis (Figures 3 and 4) resulted in a well-defined pattern clustering the keywords into four groups, with colored lines indicating strong co-occurrence links between them. In the network mapping shown in Figure 3, (*a*) the first cluster (red color) comprises the keywords "*Aspergillus flavus*," "biological control," "climate change," "deoxynivalenol," "food safety," "*Fusarium graminearum*" and "mycotoxins"; (*b*) the second cluster (green color), includes "aflatoxin B1," "aflatoxin M1," "aflatoxins," "biocontrol" and "maize"; (*c*) the third cluster (light blue color) encompasses "detoxification," "exposure," "margin of exposure," "risk assessment" and "toxicity"; while (*d*) the fourth cluster covers "*Aspergillus*," "fumonisins," "*Fusarium*" and "ochratoxins." An in-depth analysis of the co-occurrence of keywords from different clusters (Figure 4) revealed "climate change" as the key element for most papers, with this keyword strongly linked (thick lines) to most of the main keywords of other clusters such as "fumonisins," "*Aspergillus*," "aflatoxins," "maize," "aflatoxin B_1" and "risk assessment."

The bar graph in Figure 5 displays the top 20 countries affiliated with authors of the selected papers. Italy and the United States were the leading countries where researchers citing Battilani, et al. [17] and Battilani, et al. [18] came from, with 38 and 27 papers, respectively. There were also scientists from the United Kingdom (14), Croatia (13) and Austria (11) together with Hungary and Serbia. This top 20 highlight a deficit of papers from some continents where mycotoxin contamination is considered a major problem, with implications that affect human and animal health (i.e., Africa and Asia). Indeed, only Nigeria (4 papers) and China (9 papers) ranked in this top 20 list. The pie chart (Figure 5—upper corner right) illustrates the authors' countries for the 25 studies selected for quantitative analysis, considered as "reactions": Here also, Italy (7), the United Kingdom (5) and the United States (4) were the countries with the largest number of articles.

Figure 2. Treemap of all source titles for the records (paper and report citations) identified during step *I* filtering. Treemap elaborated and created using the DrasticData online tool [243].

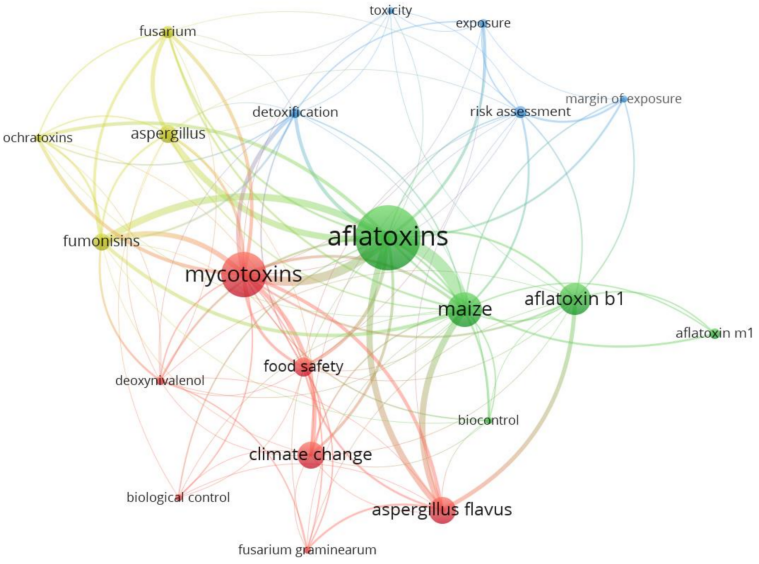

Figure 3. Scientific mapping of all keyword networks based on records (paper and report citations) from step *I* filtering.

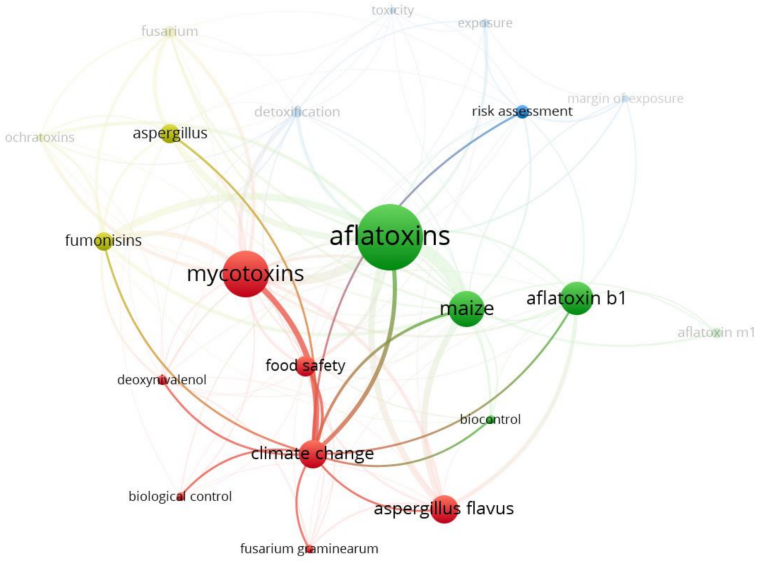

Figure 4. Scientific mapping of strictly linked networks for climate change as keyword, based on records (paper and report citations) from step *I* filtering.

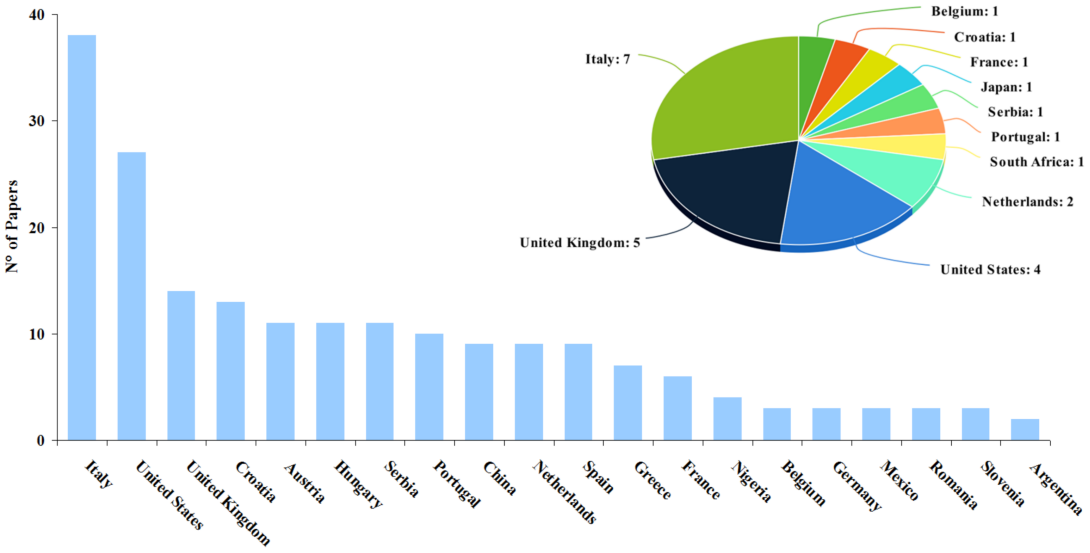

Figure 5. Bar graph showing the top 20 countries affiliated with authors of records from step *I* filtering. [Others: 3 papers each from Belgium, Germany, Mexico, Romania, Slovenia; 2 papers each from Argentina, Canada, India, Iran, Malawi, Malaysia, Philippines, Poland, South Africa, Switzerland, Thailand, Turkey; 1 paper each from Algeria, Brazil, Cyprus, Egypt, El Salvador, Ghana, Haiti, Indonesia, Ireland, Japan, Lithuania, North Macedonia, Pakistan, Saudi Arabia]. Pie chart (upper corner right) refers to the authors' countries for the 25 studies selected for quantitative analysis.

4. Reactions

We selected 25 papers from the final dataset, accounting for the scientific community's reactions to the topic (Table 1). The eligible research studies were tabulated, according to study area, matrix, model approach, weather data, climate scenario, current and future impact, and mycotoxin occurrence and co-occurrence, in order to highlight the availability of data and to outline some statements based on the above-mentioned tabulating criteria. Most of the matrices analyzed were related to both food and feed (general), while maize was the most represented crop. Milk and dairy products were also present, as well as coffee, tomato, grapes and wheat. The majority (64%) of studies did not implement any models, such as climate models, plant phenology or algorithms, or just referred to the results published in other studies. As expected, most of the work was focused on AFs

(AFB_1, AFM_1 and total AFs), while their co-occurrence with other mycotoxins (FBs and DON) in the same matrix was only considered in two cases. The analysis of the impact of current climate conditions on mycotoxin contamination was limited to six studies, which was further reduced to three studies if the assessment of the impact of future climate scenarios was also studied.

4.1. CC Impact on Aspergillus flavus and Aflatoxin Contamination

First confirmations of the predicted increase in risk of AFB_1 occurrence in maize under CC scenarios arrived soon after publication of the MODMAP-AFLA report in 2012 [17], with an event occurring in Serbia in the same year [244,245]. This was also the case for France, where, in 2015, exceptionally hot and dry climatic conditions caused 6% of maize fields to be contaminated by aflatoxins. Strains of *Aspergillus* section *Flavi* were isolated from maize samples, and *A. flavus* was the prevalent species (69% of strains), confirming the presence of these potent toxin-producers in fields in France [31], in addition to those reported in Italy before [13,246] and after publication of the report [247].

The same approach reported in the reference papers [17,18] was used effectively to study the outcome of CC on *A. flavus* in maize in Malawi [248]. Malawi is projected to get warmer (by 1–2.5 °C) and drier (reduction of 0–4% in annual rainfall levels) in all regions, with some uncertainty regarding precipitation. These conditions are expected to shorten the maize growing season, with a major impact on long-development varieties, causing the pre-harvest conditions for Malawian maize to become more favorable for AFB_1 contamination. This was the only study that considered all components of CC, with particular regards to the effect of climate on maize crop phenology, *A. flavus* ecology and expected AFB_1 contamination of grain.

The effect of CC was also reviewed in the context of mycotoxigenic fungi in coffee cultivation regions, Mesoamerica and central Africa in particular [21]. CC is expected to modulate the prevalence of fungal species, with a decline in *Penicillium* species and an increase in aflatoxin-producing *Aspergilli* species. In addition, the impact on OTA production seems species dependent. In fact, only for *A. westerdijkiae*, high CO_2 (1000 ppm), high temperature (30–35 °C) and sub-optimal a_w (0.90, 0.95 and 0.97), significantly stimulated OTA production in coffee beans. Suitable coffee growing areas will be affected by CC as well. Predictions suggest that suitable coffee cultivation areas could decrease by ~50% by 2050, both for Arabica and Robusta varieties. All indications showed that CC will have an extremely negative effect on future coffee production worldwide, in terms of both loss of cultivation areas and increase in mycotoxin contamination. In particular, suitable areas will migrate to higher altitudes where temperatures are cooler. Generally, Arabica is expected to fare worse than Robusta. However, more research is needed to understand how shifts in suitable areas for Arabica and Robusta will impact fungi and their mycotoxins under various CC scenarios.

An interesting approach evaluated grain contamination and considered the impact of CC on the maize-milk chain. This case study was based on maize grown in eastern Europe and imported to the Netherlands to be fed—as part of compound feed—to dairy cows. Three different climate models, one AFB_1 prediction model and five different carryover models (carryover intended as the passage from AFB_1 in the feed to AFM_1, its hydroxylated metabolite, in the milk) were used and combined to obtain a predictive tool based on Monte Carlo simulations [191]. The results showed that, given the case study and the scenarios and models used, AFM_1 contamination in milk is expected to be comparable or to increase in future climates. The outputs were sometimes in disagreement, depending on the model used; nevertheless, this study merits attention for the chain approach suggested.

The exposure of Serbia's adult population to AFM_1 from milk and dairy product consumption in 2015–2018 was examined by Djekic, et al. [64] and confirmed the previous data. In fact, these authors showed a moderate exposure risk compared with similarly managed studies worldwide, but the research underlined the importance of promoting

continuous monitoring of feed and dairy supply chains and providing exposure assessment updates, with the exposure variable depending on the monitoring year.

However, all the studies mentioned above were missing essential aspects of fungal and plant interaction. Medina, et al. [128] stressed this critical aspect, underlining the importance of ecological studies to assess how fungal resilience is affected by interacting CC factors. Camardo Leggieri, et al. [45] recently confirmed this concern by using maize grown in 2014 in northern Italy as a case study. Wide unevenness in mycotoxin occurrence was noticed, even within a small area, with changes in the prevalent compound and in the level of contamination. This variability was attributed to CC effects on fungal complex interaction, with the dominant fungal species alternating during the growing season.

The challenging topic of defining the impact of fungal co-occurrence under different meteorological/ecological conditions on mycotoxin contamination was addressed by Giorni, et al. [249], and Camardo Leggieri, et al. [44], respectively, in field and in vitro. *A. flavus*, *F. verticillioides* and *F. graminearum* were artificially inoculated on maize grown in northern Italy in the two-year period 2016–2017. In parallel, *A. flavus* and *F. verticillioides* were inoculated on cornmeal medium and incubated under a wide range of temperature and water activity (a_w) conditions. Therefore, fungal interactions could be observed under natural conditions, but the impact of temperature and a_w could also be studied in detail and modeled. Under natural conditions, AFB_1 accumulation was stimulated by the presence of *F. graminearum*, while no effects on FBs or DON, caused by *F. verticillioides—F. graminearum* co-occurrence were noticed. Interestingly, the co-occurrence of *A. flavus* with *F. verticillioides* or *F. graminearum* significantly reduced both FBs and DON production. Only *A. flavus* and *F. verticillioides* were included in the in vitro study, and each fungus was affected by the co-occurrence of the other; in particular, showing a decrease in colony diameter of 10%, and 44%, respectively, when they were grown together compared with growth alone. On the contrary, the dynamics of toxin production under different temperature regimes followed a similar trend for fungi grown alone, or together, but with a decrease in production rate and a shift in optimal temperature for AFB_1 production. Although these preliminary results seem in partial disagreement, they need attention and careful elaboration. They provide basic knowledge for inclusion in predictive models to account for fungi co-occurrence in the CC scenario and to predict resulting mycotoxin co-occurrence.

Several researchers underlined the importance of acquiring detailed data in vitro on fungal responses to ecological conditions in the context of CC. In particular, Giorni, et al. [211] studied the effect of temperature and relative humidity on *A. flavus* sclerotia sporulation; data obtained were used to develop equations included in the AFLA-maize predictive model [16,204].

A step forward in ecological study was explored by Magan and Medina [121]. They examined the relationship between three-way interacting environmental factors, representative of CC scenarios (water stress × temperature + 2/4 °C × elevated CO_2 650/1000 ppm) on growth and mycotoxin gene cluster expression for *A. flavus.* This impacted significantly on AFB_1 production both on maize based medium (around 80 x the control) and on maize grain (x 3–4 the control). Studies on species of the *Aspergillus* section *Circumdati* and *A.* section *Nigri* on maize grain and coffee suggested that, while fungal growth may not be significantly affected, mycotoxin production seems to be stimulated by CC factors, Comparable conclusions were reported by Raiten and Aimone [157], based on ecological studies with a CC perspective on maize grain and coffee. Apart from revealing the up- or down-regulation of genes, a genomic approach represents a powerful tool for exploiting relative toxin production under extreme stress conditions, such as CC scenarios.

Most of the research efforts during recent years have focused on harvest or post-harvest contamination of AFs in feed/food commodities, but the soil ecosystem has been poorly considered. Fouché, et al. [78] recently reviewed studies that addressed the environmental and toxicological consequences of AF contamination, with the aim of clarifying the eventual risk that AF contamination poses to soil ecosystems. Many aspects of AF occurrence, degradation and the effects of its transformation products in the soil environment

are still unknown and remain an essential area of research for both soil health and soil productivity. In terms of soil moisture and air temperature changes, a climatic approach is important for future risk assessments of AF contamination.

4.2. CC Impact on Other Pathosystems

Following the prediction of CC impact on *A. flavus* and AFB_1 in maize under CC scenarios, another pathosystem, *Alternaria* spp. in tomatoes and related mycotoxins, was analyzed, this being an emerging matter of concern. Van de Perre, et al. [241] evaluated the effect of CC in two regions, Badajoz in Spain and Krobia in Poland. There was a significant difference in the potential growth of Alternaria among time frame scenarios in Poland, with far future > near future > current time frame. The results suggested that Poland's situation in the far future (2081–2100) will become similar to Spain's situation in the present time frame (1981–2000), showing a geographic shift in the problem. There were no significant differences among the scenarios studied for Spain because the higher temperatures predicted will become limiting for *Alternaria* spp.

Similarly, DON production in wheat was assessed for north-western Europe, indicating that both flowering and complete maturation of wheat will be earlier in the season because of CC effects. At the same time, DON contamination was expected to increase in most of the regions studied, raising initial concentrations by up to three times [242]. *Fusarium* species involved in Fusarium head blight (FHB) of cereals in the CC context were also addressed by Moretti, et al. [131] in 2019. In-depth modifications to the profile of toxigenic *Fusarium* species occurring on kernels at maturity in different global geographical areas are expected. A substantial modification in mycotoxin occurrence profile will most likely cause the advent of new mycotoxin risks in specific regions due to the shift of *Fusarium* species into new environments.

The CC scenarios examined by Cervini, et al. [48], considering an increase of more than 2.5 times CO_2 concentration in the northern Apulia region (southern Italy), predicted an increase in colonization rate by *A. carbonarius* and ochratoxin A (OTA) production in grapes, a matter of concern in that Italian region. Furthermore, preliminary evidence indicated that temperature increase, likely to happen in the same area, may reduce both berry spoilage caused by *A. carbonarius* and OTA production in grapes [47]. In particular, with a temperature range 18/31 °C and under water stress conditions (0.93 a_w), the fungal growth rate was slower than at 0.99 a_w, but an over-expression of OTA genes was observed. On the contrary, at 20/37 °C a higher growth rate was observed at 0.93 a_w. Therefore, high T and water stress seem not favorable for OTA production. Predictions of CO_2 and temperature increase, resulting from CC seem to lead to contrasting results that need to be verified in the future.

Overall, in the context of ecological studies, only one work [85] addressed the resilience of non-toxigenic strains of *A. flavus* to CC factors to ensure they have the necessary ecological competence to compete effectively and reduce toxin contamination pre- or post-harvest. The efficacy of non-toxigenic strains in controlling AFB_1 production was supported by expression of target structural and regulatory genes; they maintained biocontrol of AFB_1 contamination under elevated CC interacting factors (37 °C × 1000 ppm CO_2 and drought stress).

4.3. CC Impact on Human and Animal Health

During recent years, research has focused on studying or reviewing CC impact on fungal behavior and toxin production, as well as on related human health risks. Fanzo, et al. [72] examined the relationships between CC, diets and nutrition through a food system lens. They included food safety issues that were not only focused on mycotoxins, and identified adaptation and mitigation interventions for each step of the food supply chain to move towards a more climate-smart, nutrition-sensitive food system. The authors proposed that climate-smart agriculture is a promising approach for mitigating direct CC constraints. However, more action is needed to link climate-smart approaches to

diets and nutrition, especially for the most vulnerable individuals in the population. Hiatt and Beyeler [94] provided a review synopsis of what is known about CC-induced exposure and its relevance for cancer events. Considering the predicted increase in AFs with CC, of etiological importance for liver cancer, no evidence of increases in hepatocellular cancer associated with CC has been directly attributed to AFs.

The food system appears to show good resilience to CC, but this is apparently not the case for livestock, where two specific and possible impacts on the production system were underlined: (i) contamination of livestock feed by mycotoxins; and (ii) animal health under heat stress (HS) conditions [118]. This suggests the importance of linking feed safety with the integrated approach proposed to adequately tackle food safety risks associated with CC, including perspectives from different natural and social sciences [30]. The potential consequences of an incompletely explored perspective of CC must be considered.

Taking account of the impact of CC as a whole on social and environmental health elements, and of the increased risk of adverse health effects, especially on the most vulnerable groups in the population, such as children and the elderly, the Symposium "Health and Climate Change" was organized in Rome in 2018 as a joint initiative of the Italian Institute of Health and EFSA. The meeting aimed to promote an inter-sectoral and multidisciplinary approach to CC-related events to counteract expected adverse health effects; the launch of the International Charter on Health and Climate was the concrete output [159].

5. Steps Forward and Perspectives

On a global level, CC is expected to have significant impacts on plant biogeography and fungal populations, with effects on mycotoxin patterns, as confirmed by predictive approaches and field surveys. AFB_1 is expected to increase in Europe as a result of CC; this prediction is based on the AFLA-maize model and confirmed by field surveys. This result has captured the scientific community's attention, as confirmed by the numerous citations gained by the papers reporting this data [17,18].

Predictive models have become crucial for addressing future uncertainties and highlighting risk conditions on a geographic basis. They are likely to be essential tools for mycotoxin prediction, in production chain management and as support for all stakeholders, farmers, extension services and policymakers [250,251]. Scientific mapping of keyword networks of papers citing the EFSA project results [17,18] revealed the total absence of "*crop modeling*" as a keyword, although the studies analyzed contemplate most of the topics for a holistic approach. In fact, advances in modeling the impact of CC were very limited, as detailed in "*reactions*". This is undoubtedly one of the areas where research needs to be encouraged, together with extension to crops other than maize, as pointed out by Van Der Fels-Klerx, et al. [190], as well as other interacting factors, such as insects pests [252]. Furthermore, when evaluating the pressure risk of mycotoxins based on CC, we strongly advise not neglecting a pre-analysis of the suitability of countries/study areas for cultivation and the specific crop for which the current and future impact of mycotoxins must be assessed.

An increased risk of AFs is paired with fungal and related mycotoxin co-occurrence. The modeling approach should therefore include this event. Scarce data is available on this topic, and it is apparently not easy to interpret and convert into quantitative models. Therefore, new efforts should be addressed towards this research field, possibly integrated with the support of omics methodologies.

The top 20 authors' countries identified Italy, the USA and the UK as leading actors in this area, but surely does not reflect the main countries where AFs are a matter of concern for people's health, as highlighted very recently [155]. Therefore, major involvement of developing countries in studies aimed at predicting the impact of CC on AF occurrence is strongly desirable.

Several aspects related to AFB_1 and CC need more attention, based on our literature review; nevertheless, interesting statements can be captured, which can be summarized using the following keywords: *chain and multi-actor approach*, *intersectoral and multidisci-*

plinary, *resilience*, *human and animal health*, *global vision*. To further summarize, the food system should be considered as a whole [253], taking advantage of smart agriculture [23]. We can learn from each other, both from different steps in the chain and from different geographic areas. Scenario analyses build on multi-actor, intersectoral and multidisciplinary approaches, which can provide all stakeholders, policymakers and risk managers the best support in facing health threats, related to CC, and build the needed resilience.

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