



# **Fusarium Head Blight, Mycotoxins and Strategies for Their Reduction**

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**Abstract:** Mycotoxins are secondary metabolites of microscopic fungi, which commonly contaminate cereal grains. Contamination of small-grain cereals and maize with toxic metabolites of fungi, both pathogenic and saprotrophic, is one of the particularly important problems in global agriculture. *Fusarium* species are among the dangerous cereal pathogens with a high toxicity potential. Secondary metabolites of these fungi, such as deoxynivalenol, zearalenone and fumonisin B1 are among five most important mycotoxins on a European and world scale. The use of various methods to limit the development of *Fusarium* cereal head diseases and grain contamination with mycotoxins, before and after harvest, is an important element of sustainable agriculture and production of safe food. The applied strategies utilize chemical and non-chemical methods, including agronomic, physical and biological treatments. Biological methods now occupy a special place in plant protection as an element of biocontrol of fungal pathogens by inhibiting their development and reducing mycotoxins in grain. According to the literature, Good Agricultural Practices are the best line of defense for controlling *Fusarium* toxin contamination of cereal and maize grains. However, fluctuations in weather conditions can significantly reduce the effectiveness of plants protection methods against infection with *Fusarium* spp. and grain accumulation of mycotoxins.

**Keywords:** mycotoxins; *Fusarium* spp.; cereals; scab; plant protection; pre-harvest strategies; post-harvest strategies

# 1. Introduction

Mycotoxins are secondary metabolites of microscopic fungi, which commonly contaminate cereal grains (wheat, barley, oat, rye, maize and rice) and cereal products, as well as other food products [1–3]. Animal feed is one of the main sources of mycotoxins. This topic is particularly important because toxins cause mycotoxicosis of animals and remain in food products obtained from infected animal organisms. Therefore, meat and its products, milk and its products and eggs may also pose a serious threat to human health. Mycotoxins exert various effects on the human and animal bodies, among others they are mutagenic, teratogenic and estrogenic [1-6]. They also have a significant impact on the economy because, in accordance with the provisions of the legal acts, the presence of mycotoxins at a certain level results in the exclusion of agricultural crops, feed and food products from commercial trade [7]. Contamination of small-grain cereals and maize with toxic metabolites of fungi, both pathogenic and saprotrophic, is one of the particularly important problems in global agriculture. This is evidenced by numerous literature references and reports of the European Commission [1,8–10]. *Fusarium* species are among the dangerous cereal pathogens with a high toxicity potential. Secondary metabolites of these fungi, such as deoxynivalenol, zearalenone and fumonisin B1 are among five most important mycotoxins on a European and world scale [1,3,11–15] The presence of these metabolites in the grain is the result of the development of *Fusarium* head blight (FHB or scab). Epidemic occurrence

of this disease is the cause of significant economic losses because infestation of heads and panicles of cereals and maize by *Fusarium* spp. leads to a significant reduction in the size and quality of grain yield [12,16–18]. The level of contamination of cereal grain with *Fusarium* mycotoxins depends on many factors, among others weather conditions, cultivation system, method and date of grain harvest, as well as the degree of resistance of cultivated varieties to *Fusarium* spp. infection [18–22]. Considering the above, great emphasis has been put in recent years on developing effective methods reducing FHB occurrence and contamination of grain, feed and food with mycotoxins, and especially on the application of non-chemical methods.

## 2. Occurrence and Harmfulness of Fusarium spp. for Cereals

Fungi of the genus Fusarium infest cereals cultivated all over the world, but the occurrence of individual species depends on climatic conditions, mainly on temperature and humidity [1,2,23–25]. Fusarium graminearum Schwabe usually occurs in warm and hot climate regions, with an average annual temperature above 15 °C, but it is also commonly found in temperate climate countries in the growing seasons characterized by higher temperatures and high humidity. F. graminearum is recognized as the main cause of cereal head blight and maize ear rot in many countries of North and South America, as well as Southern Europe and Asia [1,17,26–31]. Fusarium fujikuroi Nirenberg is also considered a thermophilic species, and high levels of maize ear infection by this fungus and accumulation of fumonisin are often observed in hot and dry vegetation seasons [32]. Fusarium avenaceum (Fr.) Sacc., Fusarium culmorum (Wm.G.Sm.) Sacc. and Fusarium poae (Peck) Wollenw. species usually infect cereals in colder regions [1,23,24,33–35]. F. avenaceum usually occurs in areas with an average annual air temperature of 5–15 °C and moderate rainfall from 500 to 1000 mm per year or high, above 1000 mm, however, this species shows significant tolerance to temperature and humidity. F. culmorum is also tolerant to changing thermal conditions, although the harmfulness of this fungus to cereals is greater at higher temperatures [19,23,26]. According to various authors, F. poae can colonize cereal heads even in dry weather conditions [23,35–37].

Grain is the primary inoculum source of fungi causing cereal fusariosis [38–40] and post-harvest residues remaining in or on the soil, where these fungi can survive in the form of saprotrophic mycelium, and some species also in the form of chlamydospores [17,22,38,41]. Weeds, which are the hosts of fungi of the genus *Fusarium*, are an additional source of cereal infections [42,43]. Simplified soil cultivation increases the amount of crop residues on the soil surface and leads to an increase in the inoculum quantity of these fungi. Hence, the widespread use of this type of cultivation minimum tillage system may be the reason for the increase in the level of *Fusarium* spp. cereal infections [17,22,41].

Species of the genus Fusarium are the cause of pre-emergence and post-emergence death of cereal seedlings, foot rot and head blight. From a toxicological and economic point of view, Fusarium head blight (FHB) is the most dangerous disease, accompanied by mycotoxin grain contamination. *Fusarium* spp. infect cereal heads at different times, but the most susceptible to infection by these fungi are cereals in the flowering stage and immediately after flowering, especially in warm and humid weather conditions, and abundant dew and prolonged rainfall during this period [18,38,44,45]. Disease symptoms on infected head are visible during the milk maturity stage of the grain. Spikes infected by Fusarium spp. become all white or in individual fleurs. Pink or salmon-colored sporodochia with conidial spores, as well as mycelium layer, appear on infected chaff in spikes during persistent high humidity, after a few days of infection. Dying of infected spikelets inhibits the development of kernels, which causes grain number reduction in the spike. The remaining kernels developing in infected heads are usually smaller, gray, shriveled, with a loose consistency and often covered with sporodochia and Fusarium spp. mycelium [18,38,46]. Damage to starch granules and changes in storage protein composition were observed in kernels infected by *Fusarium* spp. [47–49]. The ability of these fungi to produce mycotoxin is a very important factor determining the harmfulness of *Fusarium* spp. and reducing grain quality [3,18].

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*Fusarium* head blight (FHB) is one of the diseases causing the greatest worldwide damage to cereals, especially wheat [13,17]. Oat panicles are often less affected by *Fusarium* spp. compared to heads of other cereal species [39,50,51]. However, there are regions where oat panicle blight is a serious problem in favorable weather conditions, including Scandinavia [19,35,52]. and Canada, where panicle infection in 2006 reached 40% [50]. An epidemic development of *Fusarium* diseases of the heads and reduction of grain yield even more than 50% occurrs in conditions favorable for head infections by *Fusarium* spp., i.e., high humidity, elevated temperature (above 20 °C) and the presence of fungal inoculum and cereal cultivation on large areas [13,17,38,53]. Losses resulting from the epidemic FHB development in the USA in 1993-2001 were estimated at about 7.67 billion USD [17].

Several species can cause head blight, although F. graminearum, F. culmorum and F. avenaceum are the predominant pathogens in most regions of the world [18,25,30,34,53–57]. In recent years, an increase in the significance of FHB caused by *F. poae* has been observed, which, by infecting cereal heads and panicles, does not cause fusariosis-like etiological signs and symptoms, and does not significantly affect kernel germination capacity, but contaminates the grain with mycotoxins [46,56,58,59]. However, other species, like Fusarium sporotrichioides Sherb., Fusarium crookwellense L.W. Burgess, P.E. Nelson & Toussoun, Fusarium roseum Link (syn. F. cerealis (Cooke) Sacc.), Fusarium equiseti (Corda) Sacc., Fusarium tricinctum (Corda) Sacc., Fusarium oxysporum Schltdl. and Fusarium langsethiae Torp & Nirenberg, can play significant roles in pathogenesis when weather conditions are not favorable for growth of the main FHB casual agents. The species: Fusarium acuminatum Ellis & Everh., F. fujikuroi, Neocosmospora solani (Mart.) L. Lombard & Crous (syn. F. solani (Mart.) Sacc., Fusarium incarnatum (Desm.) Sacc. (syn. F. semitectum) were also observed on heads of cereals [14,51,53,60–64]. In the case of infection of the maize ear with Fusarium spp., two diseases were described "red ear rot"—Gibberella ear rot (mainly caused by F. graminearum, F. culmorum and F. avenaceum), and "pink ear rot"—Fusarium ear rot, (mainly caused by *F. fujikuroi* and other species from *Liseola* section) [65]. Compared with "red ear rot", "pink ear rot", occurs under hotter and drier conditions, especially after pollination [66].

Each species of the genus *Fusarium* has a specific profile of toxic secondary metabolites that have phytotoxic and zootoxic effects [35,67]. The following chemotypes were distinguished in *Fusarium* spp. based on the profile of produced secondary metabolites: chemotype I—strains producing deoxynivalenol (DON) and/or its acetyl derivatives and chemotype II—producing nivalenol (NIV) and/or 4 acetylnivalenol (4ANIV). Within DON chemotypes, chemotype IA producing 3-ADON and chemotype IB producing 15-ADON were distinguished. Studies in this area have indicated that chemotypes producing deoxynivalenol and 3-ADON and 15-ADON are generally more virulent in relation to plants, and those that synthesize nivalenol are less virulent [68–70]. There are also opinions that chemotype harmfulness also depends on the host plant [63,71]. Deoxynivalenol-producing chemotype is more commonly found in Asia and Europe, although the occurrence of individual chemotypes is also modified by weather conditions [25,70,72].

A chemotype was distinguished consisting of strains capable of producing zearalenone within *F. culmorum* strains, based on PKS4 and PKS13 gene sequences, representing the ZEA cluster [73].

In the populations of individual species, both non-pathogenic strains to plants are found as well as those characterized by high virulence, leading to rapid tissue necrosis, which is often associated with the presence of genes encoding mycotoxin formation in the genome of these fungi [44,74–78]. It has been shown that cereal virulence of many species of the genus *Fusarium* largely depends on the synthesis of trichothecene compounds, especially deoxynivalenol and its acetyl derivatives and enzymes degrading cell walls of the host plant, mainly cellulases, chitinases and xylanases [68,69,79,80].

#### 3. Fusarium Mycotoxins and Their Impact on Animal and Human Health

The effect of mycotoxins on the body can be chronic (chronic toxicity) or acute (acute toxicity) depending on the dose and duration of exposure to toxins [81]. Disorders in the metabolism of proteins, fats and carbohydrates occur most often, leading to disorders in the synthesis of nucleic acids, which

in turn can contribute to kidney and liver damage, as well as cancer development [82,83]. Economic effects of feed and food contamination with mycotoxins are very significant, they increase the costs of health care and veterinary care, reduce animal production, and can also lead to the loss of human and animal life. Species of the genus *Fusarium* most frequently produce trichothecene compounds, zearalenone (ZEA) and fumonisin in cereal grain (Table 1), which pose the greatest threat to human and animal health [84–86].

# 3.1. Trichotecenes

Trichothecene compounds are classified as tetracyclic sesquiterpenes [87]. Sixteen genes involved in the synthesis of trichothecenes have been distinguished, most of them form the group of *Tri* genes. It contains genes that show a specific effect on trichothecene formation, i.e., *Tri5*, *Tri7*, *Tri13* and *Tri3* [73,88,89]. Trichothecene compounds were divided into four main groups (A, B, C and D) depending on chemical properties (functional groups) and fungi producing them. Trichothecenes produced by *Fusarium* spp. are included in groups A and B. Group A of trichothecenes includes: T-2 toxin and HT-2 toxin, diacetoxyscirpenol (DAS), scirpentriol (STO), 4-monoacetoxyscirpenol (MAS), neosolaniol (NEO). These metabolites are mainly produced by *F. sporotrichioides*, *F. sambucinum*, *F. poae*, *F. langsethiae* and *F. equiseti* [3,37,90–92]. Group A trichothecenes show cytotoxic and immunosuppressive effects. T-2 toxin, among others, induces oxidative stress, causing DNA damage, inhibiting protein synthesis and damaging lipids. In addition, it affects the mucous membrane of the gastrointestinal tract, causes blistering of the skin, swelling, irritation, necrosis, and even cell apoptosis [92].

Group B trichothecenes include deoxynivalenol (DON) and its acetyl derivatives—3 acetylodeoxynivalenol (3-ADON) and 15-acetylodeoxynivalenol (15-ADON) as well as nivalenol and fusarenon X (4-ANIV), which are produced in cereal grains by *F. culmorum*, *F. graminearum*, *F. crookwellense*, *F. poae* and *F. equiseti* [18,25,37,93,94].

Among *Fusarium* mycotoxins, deoxynivalenol generally most frequently contaminates cereal grains (barley, wheat, oat) and food products as well as animal feed [18,94–96]. However, in some countries, T-2 and HT-2 pose a higher risk to oat than DON [67,97–99]. DON in the human and animal body can cause inflammation of the small intestinal epithelium, which results in subsequent diarrhea. High DON doses have been found to cause vomiting, lack of appetite, weight loss and diarrhea, necrosis of certain tissues, such as the gastrointestinal wall, bone marrow or lymphoid tissue. Acting at the cellular level, trichothecenes cause mitosis and chromosome separation disorders, they can also induce programmed cell death of normal cells [67,98,99].

#### 3.2. Fumonisins

Fumonisins in cereal grains are mainly produced by *F. fujikuroi* (syn. *Fusarium verticillioides* (Sacc.) Nirenberg) and *Fusarium proliferatum* (Matsush.) Nirenberg ex Gerlach & Nirenberg). The listed species of fungi are common maize pathogens, hence the highest level of fumonisin contamination was found in maize grain and its products, although they are also found in other cereals and food products [14,100]. The presence of fungi that produce FB1 has been found worldwide, but most often they occur in warm climate and in tropical regions where maize is grown [101]. More than 15 fumonisin homologues have been described, including fumonisin A, B, C, and P, and, among them, fumonisin B1 (FB1), FB2, and FB3 are the most frequent naturally occurring. Fumonisin B1 is the most toxic form that can coexist with other fumonisin forms, i.e., FB2 and FB3. Forms FB1, FB2 and FB3 most often contaminate cereal and maize grains and food [14,102–104]. The production of fumonisin is dependent on *FUM1* gen which further expresses an enzyme complex known as polyketide synthase that catalyzes the initial step for fumonisin biosynthesis [105]. Research has shown that FB1 has neurotoxic, hepatotoxic and nephrotoxic effects in animals. However, in humans, it is classified as a potential carcinogen. Exposure to fumonisin may contribute to nervous system defects, probably due to sphingolipid metabolism disruption [4,106].

A relationship was found between the occurrence of nervous system defects and consumption of cereal products, maize in particular, contaminated with fumonisin [107–109]. Research studies have also confirmed the existence of a significant correlation between the amount of FB1 and the development of liver cancer [110]. Considering the significant health risk associated with the presence of fumonisins in food, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) set a maximum allowable daily intake of 2  $\mu$ g kg<sup>-1</sup> body weight/day for FB1, FB2 and FB3 (separately or in combination) [111,112].

## 3.3. Zearalenone

Zearalenone (ZEA) is one of the most common non-steroidal estrogenic mycotoxins produced by fungi of the genus *Fusarium* [113,114]. ZEA is mainly produced by *F. graminearum* and *F. culmorum*; this metabolite can also be produced by some strains of *F. poae*, *F. equiseti* and *F. crookwellense* [1,91,115–117]. Zearalenone is produced in the acetate-polymalonate pathway. It has been shown that many genes that encode enzymes known as polyketide synthases (PKSs) participate in its synthesis. These genes were included in type I polyketide synthases (PKSs). They are divided into PKS reducing and PKS non-reducing genes, among which the most important are PKS4 and PKS13. It is believed that the presence of the PKS4 gene indicates the potential for zearalenone synthesis by *Fusarium* spp. isolates. PKS4 encodes an enzyme that stimulates the expression of another PKS13 gene necessary for zearalenone synthesis [73,88,118].

Zearalenone is present in particular as maize, wheat, barley, oat, rye, sorghum, millet and rice contamination, which is why its distribution has a worldwide range [116]. In the body of animals, ZEA is metabolized in the liver to  $\alpha$ -zearalenol, which is more estrogenic than zearalenone [111,116,119]. Zearalenone may lead to hyperestrogenism and infertility in mammals. It has been established that low doses of this mycotoxin can affect the cycle of sex hormones in the body. In animals, including mice, pigs and cattle, ZEA can damage the reproductive organs and cause reproductive disorders [113,114]. Toxicokinetic studies prove that ZEA is absorbed in the digestive tract, and then metabolized and distributed to various parts of the body [120]. Zearalenone is a competitive substrate for enzymes involved in the synthesis and metabolism of steroids, and therefore can potentially act as a factor disturbing hormonal balance [121]. There was a suggestion that elevated levels of ZEA and  $\alpha$ -zearalenol in blood serum were associated with early puberty in 6 of 17 examined girls from rural areas in Italy [122].

Human exposure, resulting from the consumption of ZEA in their daily diet was estimated at 1–30 ng/g bw/day [116]. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional maximum tolerable daily intake (PMTDI) for ZEA at 0.5  $\mu$ g kg<sup>-1</sup> bw/day [111,114].

Cereals	Country	Mycotoxins	Content (Range or Average) [µg kg <sup>-1</sup> ]	References
Wheat	Slovakia		119–3119	[123]
	Canada		100–14300	[124]
	Poland	DON	5–1671	[125]
			1600-38900	[126]
			25–2975	[9]
	Norway		86	[19]
	Poland	T-2	1–22	[9]
	Poland	HT-2	2–55	[9]
	Norway		n.d.	[19]
	Brazil	FB1	958–4906	[127]
	Serbia		750–5400	[128]
	United States		5–2210	[129]
	United States	FB2	2–249	[129]
Triticale	Poland	DON	196–1326	[9]
		T-2	2–3	[9]
		FB1	342	[9]
		ZEA	4–86	[9]
Rye	Poland	DON	0-6000	[126]
Barley	Poland	DON	76–222 (spring barley)	[9]
			54–1602 (winter barley)	
	Norway		44	[19]
	Lithuania		trace-198	[130]
	D.11	T-2	2–11(spring barley)	[9]
	Poland		1–5 (winter barley)	[9]
	Poland		8–74 (spring barley)	[9]
	Toland	HT-2	3–69 (winter barley)	
	Norway		<20–21	[19]
	Argentina	NIV	0.0002–0.0161	[34]
	Poland	FB1	101 (spring barley)	[9]
	Poland	ZEA	2–31 (spring barley) 2–19 (winter barley)	[9]

Table 1. Occurrence of mycotoxins in cereals in selected countries of the world.

Cereals	Country	Mycotoxins	Content (Range or Average) [µg kg <sup>-1</sup> ]	References
	Germany		52–302	[131]
	Poland		220–2150	[132]
	Poland	DON	67–149	[9]
	Norway		426	[19]
	Finland		870–5600	[62]
	Germany		11–192	[131]
	Poland	NIV	13–1031	[132]
	Finland		n.d87	[62]
Oat	Finland	T-2	n.d.–150	[62]
	Germany		20–244	[131]
	Poland		32–311	[132]
	Poland		9–29	[9]
	Poland	HT-2	30–651	[132]
	Poland		46–93	[9]
	Norway		117	[19]
	Germany		205–296	[131]
	Finland		n.d550	[62]
	Poland	DAS	21–980	[62]
	Poland	ZEA	5–15	[9]
	Poland	DON	6150 (2013)	[133]
	Germany		170	[134]
	Poland	NIV	300 (2013)	[133]
Maize	UK	FB1	200-6000	[135]
	Ghana	FB2	10–770	[136]
	Thailand	ZEA	900	[137]
	Croatia		2–511	[93]

Table 1. Cont.

# 4. Strategies for Reduction of Fusariosis and Mycotoxins

# 4.1. Pre-Harvest Strategies

These include all preventive measures before harvesting. Their goal is to reduce as much as possible the risk of potential contamination of crops by mycotoxin-producing fungi [138]. Agronomic, breeding and selection, biological, chemical methods serve this purpose (Figure 1).

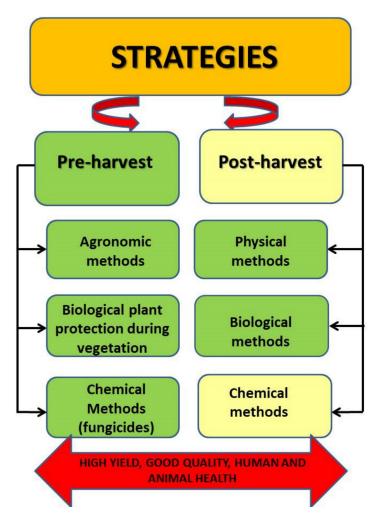


Figure 1. Mycotoxin reduction strategies.

# 4.1.1. Agronomic Methods

At present, agrotechnical measures that significantly reduce the risk of plant material contamination with mycotoxin-producing fungi are known and appreciated [139]. These include application of crop rotation, tillage, fertilization, use of appropriate quality seed material and sowing period [140]. Good agricultural practices in crop management can increase their vigor, resistance to abiotic and biotic stress factors, including susceptibility to toxicogenic fungi [141].

# Crop Rotation

Most toxicogenic fungi can survive in crop residues, therefore, properly designed crop rotation, in addition to direct and indirect protection methods (application of fungicide during flowering, use of cultivars resistant to *Fusarium* spp.) can significantly reduce the occurrence of *Fusarium* spp. and grain contamination with mycotoxins [65,142]. A particularly unfavorable form of crop rotation is cultivation of cereal plants one after another, especially after wheat and maize [17,22,143,144]. Research showed,

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that DON level in grain was high when wheat was grown after maize [124]. On the other hand, zearalenone was detected in 45% of the samples, which were collected from maize-wheat rotation [144]. Root crops and legume plants can be a more favorable forecrop, limiting the occurrence of *Fusarium* spp. in various cultivation systems [143,145]. There was a reduction in *Fusarium* head blight and DON content in wheat grown after soybean compared to wheat and maize [124,146]. The importance of the correct plant succession is high, especially when using simplified tillage methods, where a greater intensity of *Fusarium* spp. is observed [145,147]. Cultivation system, conventional and organic, also affects cereal infection by *Fusarium* spp. and grain contamination with mycotoxins, although opinions in this regard are divided [19,61,133,148]. It was found that the lack of crop rotation in conventional cereal cultivation may also lead to greater infection with *Fusarium* spp. than in the organic farming system in Norway [19].

The beneficial effect of catch crops (especialy the cultivation of white mustard) on the occurrence of *Fusarium* spp. and health of the main plant was also noted, especially in crop rotation with a predominance of cereals [149].

# Tillage and Fertilization

An important and effective way of reducing *Fusarium* heads diseases and the presence of mycotoxins in grain is soil cultivation using tillage reversing the topsoil up to 30 cm, or shallower up to 20 cm, as compared to the no-tillage system (minimum tillage system), which promotes the development of *Fusarium* spp. [19]. No-tillage or using only the chisel variant contribute to the increase of DON content in wheat grain during subsequent harvests [150,151]. Scientific research shows that the most effective method of removing crop residues from the soil surface is to use a plow with mouldboard, which inverts the soil and allows covering plant residues from the previous crop [152]. Deoxynivalenol (DON) content in wheat grain harvested from fields with minimum tillage or lack thereof was from 2.1 to 15.6 mg kg<sup>-1</sup>, and from fields plowed with mouldboard plow from 0.1 to 9.7 mg kg<sup>-1</sup>. The use of a plow with a mouldboard reduces the average DON content in wheat grain by  $33 \pm 7\%$  [152]. In addition to the soil cultivation system, tillage depth has an impact on *Fusarium* spp. The deeper the tillage, the smaller the number of isolated fungi [153]. In addition, not only plowing crop residues, especially after cereal crops, but also their removal can reduce the likelihood of infection of successive plants by *Fusarium* spp. [154].

Mineral fertilizers used in the cultivation of agricultural plants may cause higher infection degree by fungi of the genus *Fusarium*, which contaminate the yields mainly through: the rate of crop residue decomposition, rate of plant growth and change in soil structure and its biological activity [154]. Excess nitrogen in the soil increases the frequency of grain infection with *Fusarium* fungi. The type of fertilizer (urea, ammonium nitrate or calcium nitrate) can affect the degree of grain contamination with mold fungi, but not DON content [155]. In other studies, it was found that more various mycotoxins were accumulated by winter wheat grains fertilized with a higher nitrogen dose, 200 kg N ha<sup>-1</sup>, than a dose of 120 kg N ha<sup>-1</sup>. Significant statistical relationships between the concentration of mycotoxins and the amount of nitrogen fertilizer and wheat cultivar were also demonstrated [156].

# Seeds, Sowing Date and Weather Conditions

High quality seed material is an important element preventing the occurrence of pathogenic fungi, such as *Fusarium* spp. and their metabolites in plant cultivation. Seeds should be healthy, without signs of damage that could facilitate pathogen penetration, and they should have adequate viability. Various conditioning techniques can be used to improve seed viability [157]. Only high-quality seeds can compete with adverse factors during growth, such as pathogens and pests [158]. Seed physical parameters are also important, including the appropriate moisture [61].

The appropriate sowing date can also affect crop protection against pathogenic fungi. The risk of plant infection by *Fusarium* fungi, and thus contamination with mycotoxins is always greatest when the flowering period of a given plant is close to the date of fungus spore release [159,160]. It should

be noted that winter forms of cereals such as barley and wheat, developing much earlier than spring forms, are less susceptible to infection with fungi of the genus *Fusarium* [160]. In the case of maize, early sowing date in temperate climates can also contribute to protecting the crop against fungal infections of the genus *Fusarium* [161]. However, an earlier sowing date may not be effective if weather conditions are conducive to pathogenic infections [65]. The significant impact of hydrothermal conditions on the development of *Fusarium* head diseases was also indicated by studies of other authors [23,56,162]. The study of Blandino et al. [162] demonstrated that the highest maize grain mycotoxin contamination occurred in growing seasons characterized by a large amount of rainfall and lower temperatures in the period from flowering to maize maturation.

Drought, on the other hand, affects the increased occurrence of *Fusarium* in maize cultivation and the accumulation of mycotoxins, especially fumonisins [56]. Proper maize irrigation alleviates drought stress and reduces infection by *F. verticillioides* and mycotoxin accumulation, such as fumonisins, in grains [163]. However, the opposite is true in the case of wheat and small cereal irrigation, as the occurrence of FHB is increased [164].

## 4.1.2. Resistance Breeding and Varieties Selection

There are many differences in the susceptibility of particular cereal cultivars to infection by Fusarium spp., which is associated with different levels of mycotoxin contamination. These differences most likely result from different genetic pools of breeding programs in individual countries, as well as agronomic and environmental cultivation conditions [165]. Genetic modification of plants by breeding or transgenesis, and as a result cultivation of varieties resistant or showing partial resistance to *Fusarium* spp. is the most sustainable method of reducing the occurrence of this fungi and mycotoxin contamination of agricultural raw materials [160,166–168]. Several types (components) of the mechanisms of resistance of cereal heads to infestation with *Fusarium* spp. have been described, type I—resistance to infection and type II—to the spread of the pathogen in the head [169,170]. Also distinguished is type III referred to as resistance to deoxynivalenol or the ability to degrade it, and type IV consisting of plant tolerance to infection and the presence of deoxynivalenol and other secondary metabolites [171] and type V as resistance to the accumulation and degradation of mycotoxins in grain by transforming them into non-toxic derivatives or by blocking the biosynthesis of toxic metabolites [172,173]. Effectiveness in breeding cultivars resistant to fungi of the genus *Fusarium* is expedient when one considers the availability of appropriate material and tools to select the appropriate resistance line in future cultivation [174]. To achieve satisfactory success in plant breeding and transgenesis, it is important to know and understand the molecular basis of the host-pathogen relationship and plant defense responses [168]. Scientific studies showed that transgenic cereal lines, including barley, overexpressing the HvNEP-1 gene in endosperm were less susceptible to FHB infection and accumulated lower mycotoxin levels in the grain. HvNEP-1 proved to be an antifungal gene and showed strong potential as an FHB resistance gene, thereby contributing to lower mycotoxin accumulation in the grain [175].

It is now possible to identify genomic regions that contain genes, referred to as quantitative trait loci (QTLs) and single nucleotide polymorphism markers for FHB resistance derived from QTL mapping and genome-wide association studies. Ultimately, this will contribute to the selection of genotypes and cultivation of plants resistant to mycotoxin-producing pathogens [166,176].

Experimental strategies applying genomic tools that allow targeted gene silencing are increasingly being used in the current research concerning methods of *Fusarium* spp. control in cereal cultivation. RNA interference (RNAi) is a natural mechanism that regulates gene expression. Host-induced gene silencing (HIGS) is a transgenic technology used to silence fungal genes on plants during attempted infection, thereby reducing disease levels [177]. HIGS is based on the ability of the host plant to produce mobile small interfering RNA molecules generated from long double-stranded RNA that are complementary to targeted fungal genes and act as effectors and regulators of plant response to pathogens. These molecules are transferred from the plant to pathogenic fungi to induce gene silencing.

RNAi is an efficient tool that can be used in a targeted, tissue-specific manner to control mycotoxigenic fungi of crop plants [178].

The amount of mycotoxins in cereal grains can be decreased not only by reducing infection by resistant cultivars, but also by mechanisms leading to a reduction of mycotoxin accumulation, e.g., by the action of endogenous compounds on plants that inhibit their biosynthesis. These include compounds with antioxidant properties such as phenol, peptides or carotenoids and with pro-oxidative properties such as hydrogen peroxide, often referred to as mycotoxicity modulators [172].

# 4.1.3. Biological Plant Protection during Vegetation

To date, many beneficial interactions between the plant and microorganisms have been revealed that can be potentially used in agriculture, among others for enhancing defense mechanisms in plants and for biopreparation production [179]. It is extremely important to characterize endophytes and their role in agriculture, especially in plant disease resistance [179]. Bacterial or fungal endophytes can penetrate plant tissues and develop in them, thereby affecting plant growth, inducing a defensive response against pathogen attack and acting as agents preventing abiotic stress [180]. Many fungal endophytes produce compounds such as antibiotics that have antifungal, antibacterial and insecticidal properties that strongly inhibit the growth of other microorganisms, including plant pathogens [181]. It should be noted that depending on the host genotype and abiotic stress factors, some endophytes may become pathogens, as exemplified by F. verticillioides in maize [182,183].

Biological agents are an alternative to chemicals. These are factors of natural origin, which primarily include antagonistic microorganisms. Bacteria of the genera Bacillus, Pseudomonas and Lysobacter are considered as factors limiting phytopathogens [184,185], as well as fungi of the genus Trichoderma [186,187]. Strains of the species Trichoderma atroviride P. Karst., Trichoderma longibrachiatum Rifai and Trichoderma harzianum Rifai were found in the group of microorganisms capable of limiting the synthesis of Fusarium mycotoxins [188–190]. A study by Ferrigo et al. [190] suggested that biopriming of maize seeds with *T. harzianum* T22 could be a promising and environmentally friendly way to control kernel colonization by *F. verticillioides* and fumonisin accumulation. *Bacillus megaterium* (B5), B. amyloliquefaciens (B28), T. harzianum (T37) and Epicoccum sp. (E52) proved to be the most effective antagonistic isolates against wheat pathogens. In addition, strain B28 (B. amyloliquefaciens) increased the weight of 1000 wheat grains by 16.77% and was as effective as Sumi-8 fungicide [191]. It has been found that Bacillus subtilis acts as a fungal antagonist, inhibits the growth of F. verticilloides and the amount of produced fumonisins even by 50% [192,193]. Scientific research shows that some Streptomyces strains can also inhibit the development of Fusarium spp. [194,195]. A combination of biocontrol using Lysobacter enzymogenes strain C3 with a fungicide tebuconazole also provided good results in spring wheat cultivation. This combination reduced FHB incidence or severity, and thus guaranteed effective crop protection [184].

#### 4.1.4. Chemical Method

Numerous studies have found that head diseases of cereals caused by fungi species of the genus *Fusarium (F. culmorum, F. graminearum, F. avenaceum, F. poae)* and *Microdochium nivale* (Fr.) Samuels & I.C. Hallett as well as grain contamination with DON can be significantly reduced by using fungicides such as triazole, metaconazole, and tebuconazole [196,197], cyproconazole, prochloraz and a mixture of tebuconazole and azoxystrobin [198]. It should be noted that non-chemical preventive methods that are insufficient to limit the occurrence of *Fusarium* fungi are increasingly being combined with chemical methods. Such integrated actions allow to reduce the occurrence of pathogenic fungi and their secondary metabolites with higher efficiency. Scientific research shows that integrating cultivar resistance using fungicides can be an effective strategy for FHB and DON control in winter wheat. On the other hand, the application of tebuconazole + prothioconazole in combination with cultivar resistance may be a much better solution in limiting FHB and DON in grain than using breeding-resistance and chemical methods separately [199,200]. It should be noted that the use of chemicals in plant

protection increases the risk of lower quality of agricultural raw materials and products in the context of human health safety [201]. In some cases, increased DON production was found in the application of epiconazole and propiconazole [202,203] or azoxystrobin (azoxystrobin) [204].

#### 4.2. Post-Harvest Strategies

Treatment of agricultural raw materials after harvest is also important. Such actions should be aimed at limiting the risk of contamination with pathogenic fungi and mycotoxins. Physical, biological and chemical methods serve this purpose (Figure 1). In post-harvest strategies, education and training of agricultural producers in the application of various methods, including particularly good agricultural practices, limiting the amount of mycotoxins in agricultural produce, play an important role [205].

#### 4.2.1. Physical Methods

All physical activities related to grain preparation for storage can play a key role in preventing mycotoxin contamination [206,207]. After harvest, grain moisture content depends on various biological and atmospheric factors. To ensure proper storage of grains, they should be dried shortly after harvest to the appropriate moisture content. This process reduces or even prevents mycotoxin production [208]. Stacking until dryness is practiced in the case of harvesting whole plants, e.g., maize from small area by small-scale farmers in east Africa [206]. It is important then to provide adequate aeration to reduce the risk of mold fungus development. During husking (manual or mechanical), care should be taken to minimize seed damage, as this causes increased mycotoxin contamination [206,209]. Sorting, washing or grinding cereal grains is also important in reducing the amount of mycotoxins [210]. Optical sorting, introduced in the 1960s, using UV light illumination or opto-electronic sorting can be used [211]. The choice of sorting depends on the possible occurrence of mycotoxins, which do not always give visible signs [209]. An example is fumonisin, which accumulates in significant amounts, despite the fact that *F. verticillioides* often gives no symptoms [211–213]. In the case of grains infected with *Fusarium* spp., high mycotoxin concentration in the surface tissues of grains can be successfully reduced by cleaning, husking and removing residues [211]. A large proportion of mycotoxins is found in damaged grains, fine material and dust [208,214], therefore it is also recommended to clean grain surface, which ensures a better health condition, especially in preventing colonization by fungi of the genus Fusarium and accumulation of their secondary metabolites. Damaged grains are most often a habitat for spores and they may contain up to ten times higher amounts of fumonisins than intact grains [154]. Adequate humidity and seed storage temperature are also important, and when these parameters are regulated, then mycotoxin contamination due to fungal growth after harvest is very rare [215]. It should be noted that adsorbents, such as activated carbon, aluminosilicates or polymers are increasingly used, which were shown to be highly effective in removing toxins in in vitro and in vivo studies [216]. A promising procedure is the adsorption method, which uses multi-component agents such as: aluminum silicates and sepiolites, or activated carbon, capable of adsorbing 100% fumonisin B1 [217,218]. Good, although expensive effects in limiting the growth of toxicogenic fungi and mycotoxins (especially fumonisins) are brought about by the use of antioxidants and essential oils in a controlled atmosphere in the storage room [208]. Undoubtedly, the antifungal effect of ozone and arc discharge plasma as well as cold atmospheric pressure plasma also show great hope in the sterilization of seeds of various plants, including cereals [219,220].

Ozonation is a simple technology that leaves no undesirable residues [221]. It is increasingly used to prevent the development of pathogenic fungi during storage as a strategy for the balanced control of these microorganisms [222]. Ozonation significantly contributes to deoxynivalenol content reduction in wheat grain [223]. The rate of mycotoxin degradation is usually positively correlated with ozone concentration and time of grain exposure to ozone [224]. Compared to chemical fumigation, ozone fumigation has many advantages, such as rapid ozone decomposition to molecular oxygen, no residue, and the possibility of on-site production [225,226]. In addition, fumigation with chemicals is characterized by varying efficiency. Research of Solanki et al. [227] demonstrated that wheat grain

contaminated with mycotoxins, after fumigation using phosphine, still contained *Fusarium* spp. toxins, mainly deoxynivalenol. In addition, this treatment changed the structure of microorganism population, leading to a higher number of toxicogenic strains in species composition.

## 4.2.2. Biological Methods

Biological methods are also applied as part of the biocontrol of fungal pathogens and the mycotoxin neutralization in grain after harvest. Microorganisms can convert mycotoxins to non-toxic or less toxic products [228]. In order to reduce the amount of mycotoxins, biocontrol should be used in connection with good agricultural practices in post-harvest yield management [229]. Two main groups of microorganism mode of action can be distinguished—based on the adsorption and transformation of mycotoxins [230]. An interesting solution is the use of mycotoxin-binding microorganisms, especially lactic acid bacteria (LAB), but also propionic acid bacteria and Escherichia coli [231]. Literature data most often indicate the possibility of *Fusarium* mycotoxin removal by fermentation microorganisms, including bacteria that have the status of generally recognized as safe (GRAS) [232,233]. It has been shown that the mechanism responsible for the elimination of ZEA and its  $\alpha$ -ZOL derivative by various strains of *Lactobacillus rhamnosus* is the adsorption of toxins to the bacterial cell wall, and not absorption into the cell [232]. Studying the interaction between two mycotoxins, ZEA and  $\alpha$ -ZOL, and two Lactobacillus strains—L. rhamnosus strain GG and L. rhamnosus strain LC705 (used as dietary supplements), it was shown that a significant proportion of both toxins, i.e., from 38 to 46%, was recovered from the bacterial deposit, where ZEA and α-ZOL degradation products were not detected. Both heat-treated and acid-treated bacteria were able to remove toxins, indicating that binding, rather than metabolism, is a mechanism of toxin removal from the medium [232]. In another study, lactic acid bacteria (LAB), Pediococcus acidilactici, Lactobacillus sakei and Pediococcus pentosaceus strains in MRS, reduced DON content in malting wheat grain samples by 47%, and P. acidilactici and P. pentosaceus KTU05-8 ZEA content by 37-38% [234]. Čvek et al. [235], reported a high degree of adsorption of zearalenone (95-99%) by Lactobacillus plantarum A1 cells. In the case of L. rhamnosus GG, the adsorption rate was approximately 85% and 71%, depending on the amount of bacteria used per 1 cm<sup>3</sup>. Zearalenone concentration can also be effectively reduced by bacteria of the genus Brevibacillus, including B. brevis PCM 2016 and B. brevis PCM 2020 strains. The tested bacterial strains showed the ability to reduce ZEA from 12.7 to even 80.9% compared to control samples [236]. ZEA reduction by *Bacillus licheniformis* strain CK1 was over 70% (with 5 µg ml<sup>-1</sup>) at 37 °C and pH 7.0, and strain CK1 removed more than 65% of ZEA in the pH range 2.5-8.0 or at temperatures from 4 to 42 °C. After five washes, CK1 cells retained over 30% of the initially bound ZEA. These results indicate that CK1 effectively removed ZEA and for these reasons may be recommended as a future feed additive to reduce or eliminate this mycotoxin [237]. It should be noted that toxin concentration reduction by means of microbiological binding can highly vary and depends on the strain of the microorganism and the physiological state of cells [203], as well as on environmental conditions [229].

The second group of methods is based on the degradation or transformation of mycotoxins. Studies have particularly analyzed microorganisms whose metabolic activity leads to the formation of compounds with lower toxicity than the initial substance [203]. Zearalenone can be converted to conjugates such as ZEA-glycosides [238], ZEA sulfates, which are metabolites with reduced toxicity, as confirmed by the study in rats [239]. ZEA degradation in a microbiological process may result in the formation of decarboxylated or hydroxylated metabolites [203]. ZEA sulfonation by Aspergillus niger also leads to the formation of a less toxic compound [240]. There is a lot of evidence for the degradation of trichothecenene mycotoxins by microorganisms isolated from the digestive tract of cattle [241,242] and pigs [243]. Degradation occurs through two pathways—de acylation and de-epoxidation [230,244,245]. As a result of deacetylation by *Curtobacterium* spp. strain 114-2, toxin T-2 is degraded to toxin HT-2 and then to T-2 triol. Subsequently, triol T2 is deacetylated to T2 tetraol by *Curtobacterium* spp. strain BBSH 797. T-2 triol toxicity is 23 times lower than that of toxin T-2 and 13 times lower than toxin HT-2 [203,246]. Another possible transformation of trichothecenes

with the involvement of microorganisms (e.g., bacteria from the *Agrobacterium-Rhizobium* group) is hydroxyl group oxidation at position C 3 of deoxynivalenol to ketone [203,247,248]. Trichothecenes may also undergo de-epoxidation, especially deoxynivalenol (DON) and nivalenol [203], thanks to which less toxic compounds are produced [249]. Complete conversion to de-epoxy metabolites has been observed for non-acetylated trichothecenes of 4-deoxynivalenol, nivalenol and verucarol [245]. Devosia mutans 17-2-E-8 bacteria isolated from agricultural soil are able to transform DON primarily into 3-epi-DON, less toxic than DON and 3-keto-DON [250]. There is little data in the literature regarding the transformation and degradation of fumonisins. Their control using antagonistic microorganisms isolated directly from the plant microflora may be one of the options [218,251]. Research conducted by Camilo et al. [218] showed the presence of microorganisms (Gram positive bacteria and yeast), in maize and silage, capable of inhibiting the growth of *F. fujikuroi* (syn. *Fusarium moniliforme* J. Sheld.), strain 113F and fumonisin detoxification in the range from 43 to 83% of the initial fumonisin B1concentration

# 4.2.3. Chemical Methods

Strategies associated with chemical inactivation of mycotoxins include primarily mycotoxin conversion through various chemical reactions [230]. They mainly consist of the disruption or inactivation of mycotoxin by acids, bases, oxidizing and reducing compounds or chlorine compounds [207,252–254]. Good results are also obtained with organic acids such as citric and lactic acid in reducing the concentration of typical mycotoxins, especially DON and its derivative, 15Ac-DON and NIV [253]. Ammonification is the best known process for detoxification of various agricultural products [255]. Scientific research shows that the use of ammonium hydroxide also reduces the concentration of fumonisins, especially FB1 by 30-45% [154]. Hydrogen sulfates are also used, which are effective when inactivating one or more mycotoxins [230]. The use of 1% sodium hypochlorite for maize seed disinfection also reduces the occurrence of mold fungi [256]. It should be noted that the addition of any chemical substances may have a negative impact on sensory, functional and, above all, nutritional properties of crops and products prepared on their basis [257].

# 5. Conclusions

Considering literature reports, it should be emphasized that the application of single methods to reduce mycotoxin formation in cereal grains is not sufficiently effective. Therefore, combining different methods, with particular emphasis on preventive measures starting from agrotechnical methods limiting the source of primary infection, such as proper preparation of the soil for cultivation, appropriate crop rotation with the use of catch crops, selection of cultivars with a high level of resistance to *Fusarium* spp. infection, to the use of resistance inducers, including biopreparations based on antagonistic microorganisms, endophytes and biologically active substances, seems to be most appropriate. Creating the right conditions for storing grain after harvest is also extremely important. Among the post-harvest methods, the use of antagonistic bacterial strains, as well as certain physical methods, such as ozonation, provide good results.

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