Chapter 3

# *Fusarium* Mycotoxins and Metabolites that Modulate Their Production

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http://dx.doi.org/10.5772/intechopen.72874

**Abstract**

The genus *Fusarium* is a group of fungi producing several types of toxins with toxicological effect in both humans and animals. Such fungi are commonly found in soils so it can contaminate various types of crops, preferably cereals, leading to significant economic losses. Relative humidity, storage temperature and various handling in cereales increase the possibility of contamination by *Fusarium* toxins. Cereals naturally have secondary metabolites that may help attenuate contamination by these toxins, but it is necessary to know strategies and mechanisms that generate inactivation mycotoxins. This chapter reviews relevant information about cereal mycotoxin contamination, as well as the production of cereal secondary metabolites as a strategy to reduce the possibility of mycotoxin contamination.

**Keywords:** *Fusarium*, mycotoxin, secondary metabolites, cereals, detoxification

## 1. Introduction

Mycotoxins produced by fungi of the genus *Fusarium* have the universal distribution, and economic importance given their toxicity for animals, humans and plant pathogens, which infect and colonize various cereal crops such as maize, rice, wheat and oats in temperate and semitropical areas. Among the mycotoxin-producing species are *F. sporotrichioides*, *F. graminearum* and *F. verticillioides*, which produce toxins such as zearalenone, zearalene, deoxynivalenol or nivalenol, T-2 toxin and diacetoxyscirpenol [1]. These toxins generate diverse diseases to crops

and contamination to diverse types of cereals mainly to maize being of toxicological concern the ear rot [2]. Therefore, the contamination prevention could be generated by the biosynthesis the *Fusarium* during the crop. Then, the development of *Fusarium* can be triggered by the environmental conditions, agricultural practices and range of susceptibility [3]. Biochemical resistance is directly associated with specific proteins and metabolites that focus on the biosynthetic analysis of mycotoxins explaining the sporadic occurrence of the mycotoxins as fungal metabolites. Several studies indicate that secondary metabolites present in cereals can modulate the production of mycotoxins, and these are important in plant response to fungal contaminations, such as, the phenolic compounds that control or prevent the response to mycotoxins [4]. Phenolic acids, including ferulic acid, tannins and proanthocyanidins, are the most abundant in cereal showing the highest potential to function as fungal growth inhibitor [1, 3]. In this sense, the objective of this chapter is the review of the main mycotoxins of the genus *Fusarium* that affects cereals, as well as the production of secondary metabolites that can modulate their production. The above will gather relevant information on possible inhibition options in cereal contamination by mycotoxins of the genus *Fusarium*, including major mycotoxin-producing species, cereal contamination by mycotoxins (economic losses, implications to food safety and health), cereal secondary metabolites with antifungal activity and possible mechanisms that modulate inhibition of mycotoxin production of *Fusarium* species.

## 2. Overview of major mycotoxin-producing species

The genus *Fusarium* comprises an outsize cluster that includes animal and plant pathogenic species with great biological properties [5]. Some species are used as biocontrol agents, as industrially applicable enzymes, and some cause diseases in many agronomical crops and are probably the most prevalent toxin-producing fungi [6]. The genera *Aspergillus*, *Penicillium* and *Fusarium* are filamentous fungi and produce mycotoxins that are toxic and/or carcinogenic secondary metabolites produced under appropriate environmental conditions [7]. *Fusarium* produces three of the most important of mycotoxins, such as *fumonisins*, *trichothecenes* or *zearalenone*, and these furthermore produce emerging mycotoxins as well as *fusaproliferin*, *beauvericin*, *enniatins* and *moniliformin* [8].

Mycotoxins possess biological activities that represent a problem for both human and animal health (**Figure 1**). The ingestion of these compounds can cause chronic disease, morbidity and death and reduce the resistance to pathogens [9]. Most mycotoxin are stable during food processing, and these are commonly resistant to chemical and thermal changes. Mycotoxins can also come to the human by animal products [10, 11].

### 2.1. Aflatoxins

Aflatoxins (B1, B2, G1, G2) are difuranocoumarin synthesized by *Aspergillus flavus* and *Aspergillus parasiticus* present in soil and various organic materials. Aflatoxin-producing species has been reported in a wide variety of food commodities (maize, peanuts, barley oats, rice, cottonseed, spices and figs [12]. Optimal conditions for their propagation are high temperature

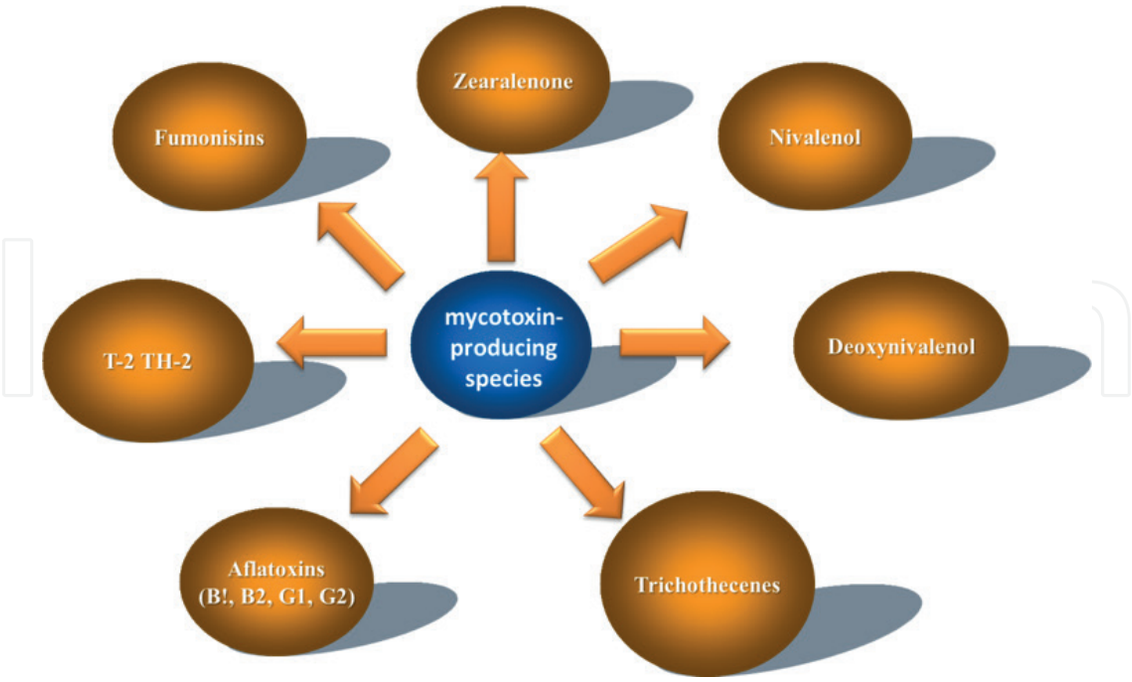


**Figure 1.** Group of mycotoxin-producing species.

and humidity (30–33°C, 0.99 water activity) [13]. Aflatoxins showed carcinogenic, teratogenic, hepatotoxic, mutagenic and immunosuppressive effects; specific limits have been set on average to 50 mg/kg for total aflatoxins.

### 2.2. Trichothecenes

Trichothecenes can be divided into four types: A (T-2 and HT-2 toxins, diacetoxyscirpenol), B (deoxynivalenol, nivalenol), C and D, and these are the main and most diverse chemical groups of the three major classes of *Fusarium* mycotoxins [14, 15]. These are shaped by a set sesquiterpenoids with or without a tricyclic nucleus. Trichothecenes are small, amphipathic molecules that can move passively across cell membranes [16, 17]. The most prevalent contaminants in wheat, barley, oats and maize are trichothecenes of types A and B. Exposure to these toxins can cause immunological problems, vomiting, skin dermatitis, hemorrhagic lesions, acute diseases and gastroenteritis. Trichothecenes in wheat behaves as phytotoxic were causing chlorosis, inhibition of root elongation, and dwarfism [4, 9]. Trichothecenes show several inhibitory effects such as inhibition of proteins, DNA and RNA synthesis on the primary metabolism of eukaryotic cells [18].

### 2.3. Deoxynivalenol

Trichothecene of type B (deoxynivalenol) is produced by *Fusarium graminearum* and *Fusarium culmorum*; these mycotoxin-producing species are found in wheat, rye, barley and oats [18]. These are a group of toxins with a keto group at carbon 8 of the parent epoxytrichothecene nucleus [19]. Deoxynivalenol is divided into five types (deoxynivalenol, 15-acetyldeoxynivalenol, 3-acetyldeoxynivalenol, fusarenon-X and nivalenol). "ribotoxic stress response" is produced

by deoxynivalenol added the ribosome in eukaryotic cells [20]. The impact of deoxynivalenol on the immune system ranges from immunosuppression to immunostimulation, according to its concentration, duration and time of exposure [19].

### 2.4. Nivalenol

Nivalenol are the main mycotoxins produced by *F. cerealis*, *F. poae*, *F. nivale*, *F. culmorum* and *F. graminearum*. Maize red ear rot throughout is caused by nivalenol [21]. As expected, they reportedly also share many toxicological properties, such as the inhibition of cell proliferation, induction of interleukin-8 secretion and the involvement of stress-activated MAPKs and nuclear factor-κB in the signal transduction pathways of toxicities [15].

### 2.5. Zearalenone

Zearalenone is a mycotoxin, which have a structure of estrogenic lactone; they have sufficient structural similarity and these synthesized by various *Fusarium* species—*F. graminearum*, *F. culmorum* and *F. crookwellense*. Zearalenone is found in cereals, mainly maize, and processed foods and these are a non-highly toxic mycotoxin [10, 22]. These mycotoxins have been producing of estrogenic effects in animals and the stimulation of human breast cancer cells growth. Zearalenone is a mycotoxin producing of host-contaminated corn [9]. Also, inhibiting the gene expression caused by zearalenone produced severe hepatic illness. Zearalenone has been shown to be immunotoxin and hepatotoxic and nephrotoxic and an enhancer of lipid peroxidation [19, 23].

### 2.6. Fumonisins

*Fusarium verticillioides* and *F. moniliforme* produced by Fumonisins (A, B, C, P) are toxic secondary metabolites, mycotoxins non-fluorescent, common fungal contaminants in grains and agricultural commodities [24]. These are analogous to sphingolipids, and intake of contaminated foods with fumonisins B1 has been associated with equine leukoencephalomalacia, porcine pulmonary edema and liver cancer in rats and decreased body weights in chickens [8, 23]. The exposure levels ranging from 0.02 to 0.2 mg/kg in body weight have been found of fumonisin concentration; these are within the limit of intake. Although fumonisins are relatively thermal stability, these may undergo reactions in food systems that alter their chemical structure and toxicity and is potentially hazardous to the health of both humans and animals [25].

## 3. Overview of mycotoxin-contaminating cereals

Mycotoxin contamination can occur pre-harvest when the crop plant is growing or post-harvest during processing. Storage of cereals at temperatures over 37°C increases humidity during prolonged storage times is a factor for crops and cereals to be susceptible to mold growth and mycotoxin contamination [16]. The susceptibility of the grain is another factor to consider, presenting greater susceptibility maize and lower rice. Animal pests, weeds and pathogens impact yield and quality of cereals. *F. graminearum* mostly affects cereals, including maize, wheat and barley. The predominant *Fusarium* species associated with ear and stalk

rots are *F. graminearum* followed by *F. verticillioides*, *F. proliferatum* and *F. culmorum* [21]. These *Fusarium* species are also capable of producing mycotoxins, which contribute to pre-harvest contamination of human food and animal feed impacting health [7]. Among *Fusarium* spp., *F. graminearum* is the most common agent causing *Fusarium* head blight [26]. The major mycotoxin type of *F. graminearum*, *F. sporotrichioides* and *Fusarium avenaceum* is the trichothecene type-B mycotoxin class of fungi capable of producing deoxynivalenol and its derivatives (3Ac-deoxynivalenol, 15Ac-deoxynivalenol) or nivalenol. The nivalenol-producing isolates of *F. graminearum* have been found to be more aggressive in maize than the deoxynivalenol-producing isolates [15]. On the other hand, maize production is mainly affected by diseases caused by the species *Fusarium proliferatum*, *F. verticillioides* and *F. subglutinans* and mycotoxin generators including fusaric acid, fusarins and fumonisins. Among fumonisins, fumonisin B1 (FB1), FB2 and FB3 are most frequently encountered in maize kernels [1, 27]. *Fusarium sporotrichioides* is a common soil-borne plant pathogen causing dry rot of potato [28].

## 4. Cereal secondary metabolites with antifungal activity

A component of the plant resistance to *Fusarium* and their toxins is related to the capacity of plant tissues to reduce the fungal infestation and mycotoxin accumulation (e.g. zearalenone, type B trichothecenes, fumonisins) throughout the presence of secondary metabolites. Secondary metabolites are compounds produced by plants for which no role has yet been found in growth, photosynthesis, reproduction or other "primary" functions; however, it has been found that they are implicated in plant defense. The presence of secondary metabolites along with temperature, water activity, pH and nutrients have been identified as key features regulating *Fusarium* and their mycotoxins [29].

Plant endogenous compounds can be both constitutively synthesized and induced in response to pathogen infection. Recent metabolomic studies have pointed an important amount of cereal metabolites produced by cereals such as fatty acids, amino acids and their derivatives, carbohydrates, amines and polyamines, terpenoids, benzoxazinoid derivatives and phenylpropanoids that contribute to the resistance of *Fusarium* and low mycotoxin accumulation (**Figure 2**). These metabolites are derived from primary and secondary metabolism [30]. Based on their biosynthetic origins, plant secondary metabolites can be divided into three major groups: phenylpropanoids, terpenoids and nitrogen-containing alkaloids. The secondary metabolites that play a role in the plant resistance to *Fusarium* and mycotoxin accumulation are listed below.

### 4.1. Phenylpropanoids

Phenolic compounds are secondary metabolites that are produced by descend from the phenylpropanoid pathway and are synthesized by plants from the amino acid phenylalanine. Plant biosynthesis produces various phenols that can be grouped commonly as flavonoids and phenolics. Flavones, flavonols, flavanones, flavan-3-ols, anthocyanidins, isoflavones, coumarins, stilbenes and lignans are the main flavonoids. These are structurally distinct because of their specific hydroxylation, methylation and conjugation patterns, with various monosaccharides and disaccharides. Phenolic acids found in cereals exist in both soluble (free) and insoluble

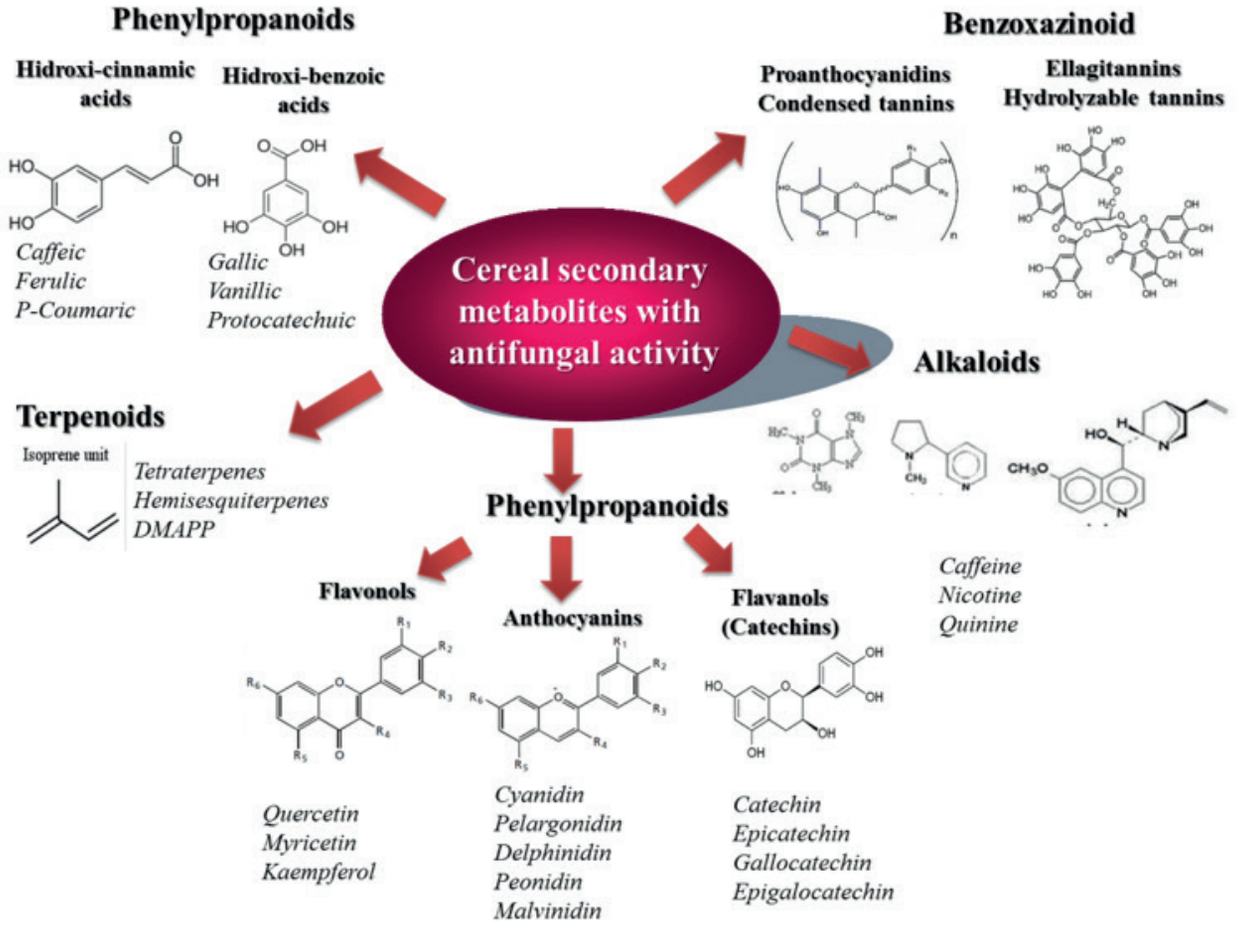


**Figure 2.** Cereal secondary metabolites with antifungal activity.

(cell wall-bound) forms [31]. The major portion of phenolic compounds is in the outer part of grains. Moreover, phenolic acids, predominantly ferulic and coumaric acid, play an important role in limiting polysaccharide degradation by exogenous enzymes, where they act as a cross-link between polysaccharides and between polysaccharides and lignin [32].

Phenolic compounds in plants are involved in the interaction between the pathogen and the plant. For example, the phenolic acids accumulated throughout the development of wheat-kernel development impact positively the resistance to *Fusarium* [33]. It has been reported the fungicidal efficiency of phenolic compound considering $IC_{50}$ values. These values rank between 0.7 and >10 mM [30].

It has been stated that the most maize-resistant genotypes exhibited high levels of phenylpropanoids, which were related to low levels of disease severity and grain fumonisin (FUMO) concentration [34]. In a study using wheat cultivars (winter and spring), significantly higher amounts of free phenolic compounds were found in the glumes, lemmas and paleas of the spring cultivar prior to and at all sampling times after inoculation, in comparison to the winter wheat cultivar. The spring cultivar exhibited resistance against initial infection by the fungus. It was found that the amount of *p*-coumaric acid increased significantly in the glumes,

lemmas and paleas of the spring cultivar concluding that phenolic compounds appear to play a role in the resistance of the cultivars to *F. culmorum* [35]. In the same way, a study with date palm roots showed that date palm roots contain four cell wall-bound phenolics identified as *p*-hydroxybenzoic acid, *p*-coumaric acid, ferulic acid and sinapic acid. The contents of *p*-coumaric acid and ferulic acid, *p*-hydroxybenzoic acid, sinapic acid and lignin in the resistant cultivars to *F. oxysporum* were about 2, 8.4, 4.5 and 1.8 times higher than those in the susceptible cultivars [36].

Regarding mycotoxin production, cinnamic acid derivatives such as sinapic, caffeic, *p*-coumaric, chlorogenic and ferulic acids are efficient inhibitors of TCTB (type B trichothecenes) production by *F. graminearum* and *F. culmorum*. It is important to mention that the effect of phenolic compounds is strain and molecule dependent [37].

An amount of studies support that phenolic compounds have a role in enhanced plant resistance to *Fusarium* [38–43]. Besides, number of studies related to phenolic acids supports that in cereals, cell wall-bound ferulic acid along with its dehydrodimers and free chlorogenic acid could be pivotal components of the resistance to toxigenic *Fusarium* species [34].

### 4.2. Terpenoids

Terpenes are the most numerous and structurally diverse plant natural products. The plethora of terpenoid compounds is biosynthetically assembled from only two simple precursors, isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP). Plant terpenoids include compounds ranging from C5 hemisesquiterpenes to C40 tetraterpenes, with diverse physical and chemical properties leading to lipophilic or hydrophilic, volatile or non-volatile metabolites [44].

Several terpenoids have their roles in plant defense against biotic and abiotic stresses, or they are treated as signal molecules to attract the insects of pollination. In a study using cyclic terpenes (limonene, menthol, menthone and thymol) against *F. verticillioides*, limonene and thymol showed the highest inhibitory effects on *F. verticillioides* development. Thymol was the most active inhibitor of fumonisin B1 biosynthesis [45].

In the last year, essential oils, which composition mainly include terpenes and terpenoids, from different plants were used in the prevention of fungi and mycotoxins accumulation in cereals. A study using *Melissa officinalis*, *Salvia officinalis*, *Coriandrum sativum*, *Thymus vulgaris*, *Mentha piperita* and *Cinnamomum zeylanicum* showed that all these essential oils have an inhibitory effect on fungal contamination of wheat seeds. This ability was dose-dependent. Regarding mycotoxin development, the best control on fumonisins production was recorded for *Cinnamomum zeylanicum* [46]. Similar findings regarding essential oils were done by Daferera et al. [47]; *Fusarium* sp. was completely inhibited by oregano, thyme, dictamnus and marjoram essential oils at moderately low concentrations (85–300 μg/mL). Also, oils from *Cymbopogon citratus*, *Ocimum basilicum* and *Ocimum gratissimum* were the most effective *in vitro*, completely inhibiting the growth of *F. verticillioides*. The application of these oils at concentrations of 8, 6.4 and 4.8 μL/g inhibit the growth of *F. verticillioides* in maize for a period of 21 days. It was also observed that the production of fumonisin was not affected by the lower concentration (4.8 μL/g) [48].

On the other hand, in a cromatografy study, volatile organic compounds (VOCs) were identified using GC-MS in oats, barley and wheat infected by three species of *Fusarium*, including species that caused cortical rot disease in wheat, and two terpenes were identified (linalool and β-caryophyllene), which found higher concentrations with respect to the controls [49].

The metabolomics as a tool helped in to identify the metabolites in barley that are related to resistance against *Fusarium* head blight FHB exposed that metabolites conferring resistance mainly belonged to phenylpropanoid, flavonoid, fatty acid and terpenoid metabolic pathways [50]. A research by Wang et al. [51] exposed a number of genes involved in secondary metabolites biosynthesis are specifically responsive to *F. verticillioides* inoculation in BT-1 kernels. Terpenoid biosynthesis and diterpenoid biosynthesis were particularly increased by *F. verticillioides* inoculation. See Ref. [29] to review a list of terpenoids conferring resistance to *Fusarium*.

### 4.3. Alkaloids

Alkaloids are a group of chemical compounds that mostly contain basic nitrogen atoms. Saponins are a class of glycosylated triterpenes; steroids and steroidal alkaloids synthesized from the mevalonate or non-mevalonate pathway in plants. These compounds are absent in most monocotyledon plants and all cereals except in oat. The glycosylated form confers activity to avenacins, contrary to other compounds such as avenacosides, benzoxazanoids and other compounds with antifungal activity, then only with active in its form of aglycone [52]. Vacuoles are the reservoir of inactive avenosides, which allow them to be available when there is tissue damage caused by pathogenic fungi causing their activation; this results in alteration of the membranes and consequently the formation the biologically active aglycone. In a research performed by the homozygous mutant, *A. strigose* lines and the wild-type line were inoculated with fungal pathogens to assess the effects of the saponin-deficient mutations on plant disease resistance. The results exhibited that mutant plants showed increased susceptibility to *Fusarium culmorum* and *Fusarium avenaceum* revealing an implication of saponins in the plant resistance [53].

The best-known alkaloids of grasses are hordenine and gramine. Hordenine is found in many plant species and in cereals; it has been reported in barley, millet and sorghum. The reports of their allelopathic effects may imply a resistance to *Fusarium* and their mycotoxins; however, no specific reports have been found.

Several compounds within the monoterpene indole alkaloid class are known to exhibit antifungal properties. Secologanin production is induced by the application of methyl jasmonate in *C. roseus*, perhaps suggesting a link between defense-related signaling pathways and monoterpene indole alkaloid production. A study using double haploid barley lines differing in *Fusarium* head blight sensitivity observed metabolite accumulation and found secologanin was constitutively produced in resistant lines [54]. Few alkaloid compounds have been identified within wheat. A more detailed understanding of how cereal crops and related grass species respond to *Fusarium* pathogens will reveal novel mechanisms of resistance.

### 4.4. Benzoxazinoid

Benzoxazinoids (Bxs) are widely distributed in cereals discovered in the 1950s. A range of biological roles such as allelopathy, resistance to insects and defense against pathogens has

been attached to them [55]. Benzoxazinoids are synthesized in the shikimate pathway from the amino acid tryptophan. They are present in maize; wheat, rye and certain wild barley species, however, have not been found in cultivated barley varieties, oat or rice. Bxs are stored in an inactive glucoside form in plant vacuoles or plastids to avoid toxicity to the plant itself; through the enzymatic activation and chemical degradation, the tissue disrupted form the active benzoxazinoid [56]. In a research using wheat, principal component analyses demonstrated a correlation between the susceptibility to FHB and the concentrations of range of Bxs [57]. The benzoxazinoid 2-β-glucopyranoside-2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA-glc), $\alpha$-tocopherol and the flavonoids homo-orientin and orientin were identified as potential inhibitors of (deoxynivalenol) DON accumulation in a study with wheat that correlates accumulation in *Fusarium*-infected winter and spring wheat cultivars [58].

A plethora of secondary metabolites have been reported to inhibit *Fusarium* and their mycotoxins; however, the molecular mechanisms of plant resistance to both are needed to provide a deeper understanding of the mode of actions of the metabolites as well as the mechanisms of detoxification.

## 5. Possible mechanisms and management that modulate inhibition of mycotoxin production of *Fusarium* species

Mycotoxins produced by *Fusarium* spp. include different compounds with trichothecenes, fumonisins, zearalenone and emerging toxins such as fusaproliferin, enniatins, beauvericin and moniliformin [10]. This mycotoxins genus can infect cereals directly during ripening, harvesting or storage, the crop soil affecting plant growth and development, which makes its eradication complex and difficult, but various strategies are used to reduce this contamination, butte the best strategies cannot completely eradicate mycotoxin contamination. Prevention strategies during cultivation and storage aim to eliminate mycotoxins; some of the strategies used are crop rotation; in this sense, Schaafsma et al. [59] observed in a 4-year study that planting a crop other than wheat 2 years previous to planting a wheat crop significantly decreased the level of DON in wheat grain in 1 year out of four. This type of studies support the theory that crop residues are the source of *Fusarium* toxin inoculum, so alternating crops would reduce the possibility of contamination. However, studies such as that reported by Fernández-Blanco et al. [25] indicate that wheat grown consecutively (each year) has less contamination by *Fusarium* toxins than alternately grown wheat. Urea fertilization is another strategy to reduce contamination by *Fusarium* sp. as mentioned by Teich [60] and Martin et al. [61], where they applied urea instead of ammonium nitrate, with fewer pollution symptoms observed. Among the aspects to consider in order reducing *Fusarium* contamination is the cultivation season, since it has been documented that winter varieties develop and mature before spring varieties, which reduce the risk of *Fusarium* infection, for avoid that flowering coincides with spore release.

Alternatives to chemical fungicides, such as biocontrol agents, have been tested extensively in both the greenhouse and field environment, but the toxins of *Fusarium* control efficacy under field conditions have not been consistent [62]. However, some of the strategies to reduce contamination at the crop level are not always effective, so at the storage level it is sought to address other types of strategies.

### 5.1. Storage

The mycotoxins generated by *Fusarium* sp. usually present with greater incidence during the storage. The conditions for the mycotoxins biosynthesis are the grain with temperature 25–32°C, moisture between 16 and 30% and air RH of 80 and 100% [63]. This is why the strategies to mitigate and inhibit mycotoxins are postharvest management and storage strategies. Postharvest management has a significant role in mitigation of mycotoxins through good management in grain food chains during harvesting, cleaning, drying, storage and processing. The control of moisture, temperature and humidity to safe storage levels laid a key to mitigate mycotoxins in grains. Ouzounidou et al. [64] indicate that reduction in oxygen and increase in carbon dioxide concentrations generate effects on the growth of fungi. Decreasing $O_2$ to minor of 0.14% and increasing $CO_2$ to more of 50% are required for inhibition of mycelial growth and will prevent mycotoxin [65]. The degree of inhibition achieved by elevated $CO_2$ concentrations is dependent on other environmental factors, such as relative humidity (RH) and temperature [66]. Irradiation is usually used as a mitigation of mycotoxins; 4–6 kGy gamma-irradiation reduces *Fusarium* toxins and was eliminated at 8 kGy [67]. Both inhibition and elimination of *Fusarium* mycotoxins can be attributed to providing energy, which results in reactions and changes molecular structures.

### 5.2. Chemical and biological control

Another strategy is the application of chemical control as fungicides; however, this application can sometimes be ineffective and even increase the production of mycotoxins [68, 69]. That is why another alternative is the use of natural products in specific essential oils and antioxidant compounds. In stored cereals, the application of natural preservatives and essential oils generate inhibition on *Fusarium* mycotoxins production is found [46]. On the other hand, the agreement of chemical compounds and natural products can generate a reduction of 90% in deoxynivalenol (DON) (*Fusarium* toxin) as reported by Magan [70] in agreeing BHA (butyl hydroxyl anisole), PP (propyl paraben), resveratrol and cinnamon oil. In relation to the use of natural compounds, a study of phenolic extract of *Spirulina* sp. reported by Pagnussatt et al. [71] indicates that the *Spirulina* LEB-18 extract led to mycelial growth inhibitions that ranged between 50% and 90% in addition, the extract inhibits production of nivalenol (NIV) and deoxynivalenol (DON) in 73%. This may be attributed to the extract composition (main constituents were gallic and caffeic acid). Apparently, these compounds act as fungal stressors when they hamper the energy abstention due to the lower glucose availability [72]. This may trigger the production of secondary metabolites to compensate and limit the apparent competition by the substrate of the medium [73].

Biological control is another strategy in the reduction and incidence of *Fusarium* toxin using living microorganism's whit *Bacillus* spp. [74], *Pseudomonas* spp. [75] and *Streptomyces* spp. [74]. The lactic acid bacteria (LAB) strains have been examined for their potential to detoxify zearalenone (ZEA) that is an estrogenic mycotoxin produced by *Fusarium* [76]. Sangsila et al. [77] showed that these strains of LAB are capable of ZEA detoxification in a range of 29.74–83%, where the strain with the best binding capacity was JM0812 with 83% at an initial concentration of ZEA of 74.7 μg/ml, followed by UM054 and UM055 with 82.78 and 81.69%, respectively.

Mycoparasitism is the mechanism by which a fungus parasitized another fungus and is used with biocontrol strategy. Many studies suggested that mycoparasitism was associated with competition for nutrients and space, generation of antibiotic and induction of systemic resistance on *Fusarium* spp. [78–80]. Competition for nutrients and space in the soil is considered to be responsible for the phenomenon of fungistasis via the inhibition of the germination of fungal spores in soil [81]. The deprivation of the resource in the soils is partly responsible for the suppressive nature of soils. When the antagonists present in sufficient quantity at the right time and place and can use nutrients more efficiently than the pathogen, this competition can be used as an effective biological control.

On the other hand, the production of metabolites toxic is another strategy used for the control of diverse strains of *Fusarium*. Dunlap et al. [82] in *B. amyloliquefaciens* AS 43.3 identified nine gene clusters encoding for the biosynthesis of secondary metabolites associated with the biological control of *Fusarium*. The application of gases like ozone is another strategy for the detoxification of mycotoxins; Li et al. [83] obtained a reduction of 57.3% in DON by ozonation, with the moisture content of 17% in wheat. The ozone is a gas, has a favorable penetration and can decompose the double bonds in organisms and further produces simple products with less double bond and low molecular weight; in addition, it can decompose to oxygen voluntarily with non-toxic residual. Other strategie is the application of photocatalytic activity of graphene/Zno hybrids can be useful to degrade DON up to 99% according to Bai et al. [84]. The information on possible mechanism and strategies that can help detoxification of mycotoxins has increased, however, the road is still long.

## Acknowledgements

We want to thank PFCE 2017 economic support for the realization of this research.

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