Potential Role and Involvement of Antioxidants and Other Secondary Metabolites of Wheat in the Infection Process and Resistance to *Fusarium* spp.

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Abstract: This article provides a summary of current knowledge about wheat metabolites that may affect resistance against *Fusarium* head blight (FHB). The mechanisms of resistance, the roles of secondary metabolites in wheat defense, and future directions for breeding are assessed. The soluble phenols play an important role in redox regulation in plant tissues and can act as antimicrobial compounds. The color of cereal hulls and grains is caused by such natural pigments as anthocyanins in the aleurone, endosperm, and pericarp layers of the grain. Phenolic acids, alkylresorcinols, and phytochromes actively participate in the defense system, whereas carotenoids show various effects against *Fusarium* species that are positively correlated with the levels of their mycotoxins. Pathogen infestation of vegetative tissues induces volatile organic compounds production, which can provide defensive functions to infested wheat. The efficient use of native resistance in the wheat gene pool, introgression of resistant alleles, and implementation of modern genotypic strategies to increase levels of native secondary metabolites with antifungal properties can enhance the FHB resistance of new varieties. Expanding the breeding interest in the use of forms with different grain color and plant organs can be a potential benefit for the creation of lines with increased resistance to various stresses.

Keywords: wheat; breeding; plant defense; *Fusarium* head blight; genetics and resistance; efficient wheat metabolites and antioxidants

1. Introduction

*Fusarium* head blight (FHB) and Gibberella ear rot, mainly caused by *Fusarium graminearum* Schwabe and *Fusarium culmorum* (W.G. Smith) Sacc., are two of the most devastating diseases of small grain cereals and corn [1]. These fungi substantially reduce grain yield and affect grain quality. Mycotoxin contamination of human food and animal feed has become a more important aspect than direct yield losses in affecting the economics of small grain production [2–4]. Many mycotoxins are produced in culture, but the most important are trichothecenes (which include deoxynivalenol [DON], also known as vomitoxin, nivalenol [NIV], HT-2 and T-2 toxins), zearalenone (ZEA), and fumonisins [5]. Consumption of grains containing trichothecenes may cause intestinal irritation in mammals, feed refusal in livestock, vomiting, skin dermatitis, and immunological problems [6]. *Fusarium culmorum*, *F. graminearum*, and *F. pseudograminearum* (O’Donnell and T. Aoki; group I) (=Gibberella coronoica) are the most devastating fungal pathogens on small grain cereals [7]. *F. graminearum* sensu lato is today the most frequently isolated causal agent of FHB worldwide [8,9]. The *F. graminearum* species complex (FGSC) includes 16 phylogenetic species: *F. graminearum*, *F. asiaticum* (O’Donnell et al.), *F. australomericum* (T. Aoki et al.), *F. brasiliicum* (T. Aoki et al.), *F. cortaderiae* (O’Donnell et al.), *F. meridionale* (T. Aoki et al.), *F. bohii* (O’Donnell et al.), *F. mesoamericanum* (T. Aoki et al.), *F. acaciae-mearnsii* (O’Donnell et al.), *F. pseudograminearum*, *F.
gerlachii (T. Aoki et al.), F. vorosii (B. Tóth et al.), F. aethiopicum (O’Donnell et al.), F. nepalense (T. Aoki et al.), F. louisianense (Gale et al.), and F. ussurianum (T. Aoki et al.) [10].

Among the several means of fighting this disease includes the use of fungicides, cultural practices, resistant cultivars, and biological agents [11]. As true of most plant diseases, host resistance is recommended as the most effective and economical method of management [12,13]. Fully resistant cultivars are not available to date, but some cultivars have usable levels of partial resistance that limit yield loss and mycotoxins accumulation [14].

This article discusses the main secondary metabolites and antioxidants of wheat that can contribute to resistance in wheat species and cultivars. Although they are contained in relatively small amounts in cereals, they can work together to enhance antioxidant efficiency and resistance to *Fusarium*.

Current information is presented regarding the contents and effects of these metabolites and antioxidants in relation to wheat species’ and genotypes’ resistance to FGSC.

2. Infection Process

Plants are constantly subjected to biological pressures that could compromise their development. Plant and pathogen interests are opposed and antagonistic, thus generating an evolutionary dynamic between the two. This is stimulated by the confrontation between the plant’s resistance and the ability of the pathogen to generate infection of the plant. Significant progress has been made in recent years toward better understanding the processes involved in FHB infection, and especially in the case of *F. graminearum* [15–17].

*F. graminearum*’s infection process includes a biotrophic phase, occurring within six hours post inoculation (hpi). The pathogen then shifts to a necrotrophic phase between 24 and 72 hpi via production of trichothecenes and cell wall-degrading enzymes [18]. *Fusarium* spp. are able to penetrate and invade a host with the help of secreted cell wall-degrading enzymes, thus enabling the pathogen to infect, penetrate, and grow through the wheat tissue. Among cell wall-degrading enzymes are important pectinases, xylanases, cellulases, feruloyl esterases, proteases, endo-peptidases, and lipases [19].

The glycogen synthase kinase gene (*FGK3*) in *F. graminearum* is known to be an important virulence factor for this pathogen [20].

The cell wall-degrading enzymes produced by *F. culmorum* and *F. graminearum* facilitate rapid colonization of wheat spikes [21]. Lipases are important for phytotoxicity of *F. graminearum* [22]. *F. verticillioides* lactamases constitute another group of enzymes in wheat, rye, and corn get part in the resistance process of fungi to antimicrobial environment [23].

Important for these enzymes to be active and function is the presence of encoding genes, such as the lactamase encoding gene *FVEG_08291* in *F. verticillioides* [23] that imparts resistance against lactams with benzoxazinoid rings produced by wheat, corn, and rye [24]. It is noteworthy that *Fusarium* spp. possess more than 40 lactamase encoding genes [23].

Infection with *Fusarium* species can result in the contamination of cereals with health-threatening mycotoxins. These are mainly type A and type B trichothecenes, such as T-2 and HT-2, or nivalenol (NIV) and deoxynivalenol (DON). *Fusarium* mycotoxins include also other toxic secondary metabolites, such as fusaproliferin, moniliformin, and enniatins [25]. Another minor *Fusarium* mycotoxin on wheat is beauvericin, which, in addition to its toxic activity in higher animals, possesses insecticidal, antifungal, and antibacterial activity [25]. Mycotoxins play an important role in the infection process. It has been found that toxin-producing ability correlates positively with the level of a pathogen’s aggressiveness [26]. DON kills the host cells by disrupting the cell membrane, thus causing cellular electrolyte leakage and an increase in cytoplasmic Ca$^{2+}$ ions that leads to imbalance in cellular homeostasis [27,28]. Increased production of such mycotoxins as DON and the emerging mycotoxin culmorin (CUL) having synergistic toxic effects resulting in increased pathogen aggressiveness and enhanced host colonization [29]. Lu and Edwards [30] revealed small, secreted cysteine-rich proteins as a common source of *F. graminearum*–wheat interaction effectors involved in triggering resistance or susceptibility between wheat and *Fusarium*. In a recent study by Fabre et al. [31] examining the aggressiveness of three
F. graminearum strains, the findings show that contrasts were based not upon the existence of strain-specific molecules, but rather upon the ability of a strain to accumulate sufficient effector protein abundance. Protein abundance variance was mostly driven by the strain genetics and part was also influenced by the host cultivar; however, strains by cultivar interactions were marginally detected, depicting that strain-specific protein accumulations did not depend on the host cultivar.

3. Plant Defense

3.1. Mechanisms of Resistance

Cultivar resistance is an important factor that may significantly affect infection of plants, and cultivated genotypes may have different mechanisms of resistance. Wheat's resistance against FHB includes many resistance mechanisms [32]. In the case of Fusarium infection, this includes the following components: type I, resistance to initial infection; type II, resistance to spread of symptoms [33]. After types I and II resistance, there also exists a type III resistance to toxin accumulation [34,35]. Mesterházy [36,37] distinguished the following components (types) of head blight resistance: I. resistance to invasion; II. resistance to kernel infection; IV. Tolerance; VI. resistance to toxin accumulation; VI. resistance to late blighting; and VII. resistance to head death above infection site. All these types of resistance are interdependent, but they are presumably based upon different mechanisms and inherited independently.

There are two types of plant protection against infection, active and passive.

3.1.1. Active Resistance

The interaction of F. graminearum with small grain cereals has been studied in various cellular, molecular, and biochemical areas. Plant defenses are based on both physical barriers, such as the cell wall and its modifications, as well as chemical defense mechanisms that are induced in response to external stimuli [38–40].

After recognizing the pathogen, the host plants’ basal defense responses lead to activation of several resistance mechanisms. These include production of reactive oxygen species (ROS), enzymatic and non-enzymatic antioxidants [41], cell wall reinforcement associated with phenylpropanoid metabolism [32], and callose deposition [42]. ROS accumulation and removal are controlled in plant–pathogen interactions by enzymatic and non-enzymatic antioxidants. Such enzymatic antioxidants as peroxidase (POX) and catalase (CAT) are involved in scavenging \( \text{H}_2\text{O}_2 \), whereas superoxide dismutase is a scavenger of \( \text{O}_2^- \) and changes this molecule to \( \text{H}_2\text{O}_2 \) in living cells [43]. The soluble phenols play a significant function in redox regulation in plants and can have an effect as antimicrobial compounds. In addition to ROS, there are several types of reactive nitrogen species (RNS), including nitric oxide (NO). In particular, this signaling molecule might be involved in defense reactions mediated by ROS, such as production of phytoalexins and polyamines, transcription activation, or cell wall reinforcement [43]. Recently, Khaledi et al. [44] found that NO production increased in ears and seedlings of wheat varieties after inoculation with F. graminearum, and a greater increase was characteristic of the more resistant variety compared to the susceptible one. Therefore, NO might be involved in wheat defense responses to the pathogenic Fusarium species and the relationship between ROS and RNS should be investigated in more detail.

ROS accumulation and programmed cell death as its consequence would be helpful defense strategies leading to reduced progress of the hemibiotrophic F. graminearum in the host tissues and increased resistance at the early time points after inoculation, when this pathogen is in its biotrophic phase [43]. Wheat plants’ secondary metabolites can play an important active role in their resistance against Fusarium spp. A wide range of secondary metabolites with both antioxidant and pro-oxidant properties (depending upon their concentrations), such as phenolic compounds, carotenoids, and linoleic acid-derived hydroperoxides, are synthesized and act as modulators of mycotoxin biosynthesis [26,45].
In addition to the induction of phenolics and phytoalexins, active plant defense also involves expression of pathogenesis-related (PR) proteins. When stimulated by various pathogens or conditions that mimic the effects of pathogen infection, the host is thought to inhibit growth, multiplication, and/or spread of the invading pathogen by synthesizing PR proteins [40,46]. PR proteins are presently grouped into 17 families based upon their protein sequence similarities, enzymatic activities, and biological functions [47,48].

Carotenoid and tocopherol effects on FHB and trichothecene accumulation are less investigated [49]. Boba et al. [50] were able in their study to decrease carotene content through the suppression of a lycopene $\beta$-cyclase gene. The suppression of this gene in transgenic flax then led to an increase in tocopherols, squalene, gibberellic acid, and menthol. An increase in Fusarium resistance was driven by these changes in the transgenics.

Table 1 reports determined contents of endogenous wheat phytochemicals and metabolites potentially involved in protection against oxidative stress caused by Fusarium spp. in wheat. Anthocyanins in wheat are based upon six aglycons–anthocyanidins, which differ only in their glycosylation patterns in attached sugar moieties and/or their esterification with phenolic acids [51]. This may be due to the antioxidant activity of anthocyanins, which is known to increase plant resistance [52].

| Compound                  | Content                                                                 | Reference |
|---------------------------|-------------------------------------------------------------------------|-----------|
| Total 5-n-alkyresorcinols | 761 bread wheat, 743 spelt, 654 durum, 697 emmer, 737 einkorn, 300–943 common wheat, 194–687 durum wheat, 545–654 einkorn wheat, 531–784 emmer wheat, 490–741 spelt wheat | [53,54]   |
| 5-n-Heptadecylresorcinol (C17:0) | 32–34 common wheat, 1.2 (T. turgidum ssp. dicoccum), 26.0 (T. turgidum ssp. turgidum) | [55,56]   |
| 5-n-Nonadecylresorcinol (C19:0) | 250–272 common wheat, 20.4 (T. turgidum ssp. dicoccum), 187.9 (T. aestivum) | [55,56]   |
| 5-n-Heneicosylresorcinol (C21:0) | 368–474 common wheat, 196.5 (T. turgidum ssp. dicoccum), 653.1 (T. aestivum), 164.4 (T. turgidum var. durum), 65.4 (T. aestivum) | [55,56]   |
| 5-n-Tricosylresorcinol (C23:0) | 84–108 common wheat | [55]       |
| 5-n-Pentacosylresorcinol (C25:0) | 26–33 common wheat | [55]       |
| Total anthocyanins         | 210 Pp grain; 430 Pp bran, 21–157 Ba, R, 78 Pp |          |
| Cyanidin-3-glucoside       | Ba 3.07, Pp 10.34, R 4.02 | [51,57]   |
| Cyanidin-3-rutinoside      | 8.42 Ba, Pp |          |
| Delphinidin-3-glucoside    | 13.68 Ba | [51,57]   |
| Delphinidin-3-rutinoside   | 33.44 Ba |          |
| Malvidin-3-glucoside       | 12.04 Ba, 0.48 Pp, 0.22 R |          |
| Peonidin-3-arabinoside     | 2.22 Ba, Pp |          |
| Peonidin-3-glucoside       | 0.88 Pp |          |
| Peonidin-3-galactoside     | 1.94 Ba, 0.58 Pp, 0.33 R |          |
| DIMBOA-glucoside           | 18 common wheat | [58]       |
| Total carotenoids          | 1.63–4.19 einkorn, 4.73–13.64 emmer, 2.69–8.38 durum, 1.62–2.98 spelt, 1.40–4.90 bread wheat | [59–61]   |
|                           | 5.47 mg $\beta$-carotene kg$^{-1}$ DM (T. turgidum var. durum) |          |
|                           | 3.3 < 1.4–6.6 > wheat grains, 3.2 < 1.6–4.7 > white wheat grains, 3.1 < 1.4–4.1 > red wheat grains, 6.0 < 4.7–6.6 > black wheat grains |          |
| Compound          | Content                                                                 | Reference |
|-------------------|-------------------------------------------------------------------------|-----------|
| α-Carotene        | 7.3–13.4 *T. monococcum*                                                | [62]      |
| β-Carotene        | 0.116 spring wheat, 0.195 einkorn                                       |           |
| Zeaxanthin        | 0.144 spring wheat, 0.351 einkorn, 0.138 emmer wheat                   |           |
| Lutein            | 1.096 spring wheat, 5.246 einkorn, 0.761 emmer wheat                   |           |
| Total phenolics   | 1499; 1545.7 mg FAE kg⁻¹ DM 559.1, 506.5–659.8 mg GAE kg⁻¹ 1265.7 < 837.0–2233.7 > wheat grains 1231.7 < 837.0–1759.0 > white grains 1401.8 < 1105.8–1850.9 > red grains 1546.4 < 1122.8–2233.7 > black grains | [60,61,63] |
| Total flavonoids  | 270.0, 236.2–319.3 mg RE kg⁻¹ DM 252 < 147–397 > winter wheat grains 241 < 147–351 > white grains 290 < 218–389 > red grains 361 < 321–397 > black grains | [61,63]   |
| Apigenin          | 2.512 control, 104.565 inoculated with *F. culmorum*                     |           |
| Kaempferol        | 6.009 control, 124.739 inoculated with *F. culmorum*                     |           |
| Luteolin          | 7.117 control, 458.404 inoculated with *F. culmorum*                     |           |
| Naringenin        | 7.115 control, 127.787 inoculated with *F. culmorum*                     | [64]      |
| Quercetin         | 6.958 control, 512.934 inoculated with *F. culmorum*                     |           |
| Rutin             | 13.764 control, 332.44 inoculated with *F. culmorum*                     |           |
| Vitexin           | 6.481 control, 148.256 inoculated with *F. culmorum*                     |           |
| Total phenolic acids | 987.3; 406.14 mg kg⁻¹ DM                                             | [60]      |
| Salicylic acid    | < 0.3–0.8 > free salicylic acid in leaves                               | [65]      |
| Protocatechuic acid | < 6.8–13.3 > bran, 9.2                                               | [66]      |
| Ferulic acid      | 270–1446; 3000 bran 194.18 grain at 10 days post-anthesis flower tissues (S) 69.9; (MR) 99.0; (R) 101; developing grains 10 days post-anthesis (S) 97.1; (MR) 122.3; (R) 126.2; 130.1–233 developing grains | [67,68]   |
| 4-Hydroxybenzoic acid | 87.3 control, 87.3 infected                                               |           |
| Gallic acid       | < 1–37 >; control 57, infected 77.3                                    |           |
| Vanillic acid     | < 30–70 >; control 26.7, infected 37.0                                  |           |
| Syringic acid     | < 1–62 >; control 30.7, infected 23                                     |           |
| α-Cinnamic acid   | < 3–83 >; control 127.0, infected 343.3                                 | [67]      |
| p-Coumaric acid   | < 1–63 >; bran 90; control 45.7, infected 44.0                          |           |
| Caffeic acid      | < 2–90 >; bran 38; control 40, infected 46.7                            |           |
| Sinapic acid      | < 2–2017 >; bran 200; control 136.0, infected 360.0                     |           |
| Chlorogenic acid  | < 10–69 >; control 38.0, infected 39.0                                 |           |
| Abscisic acid     | Increase from 86 to 154 ng g⁻¹ DW after inoculation with *F. graminearum* |           |
| Indol-3-acetic acid | Increase from 83 to 26 328 ng g⁻¹ DW after inoculation with *F. graminearum* | [69]      |
| Jasmonic acid     | Increase from 29 to 410 ng g⁻¹ FW after inoculation with *F. graminearum* |           |
| (-)-β-Caryophyllene | Increase from 9 to 104 ng sample⁻¹ after inoculation with *F. graminearum* |           |
| β-Linalool        | Increase from 12 to 405 ng sample⁻¹ after inoculation with *F. graminearum* | [70]      |
### Table 1. Cont.

| Compound       | Content                                                                 | Reference |
|----------------|-------------------------------------------------------------------------|-----------|
| (-)-Thujopsene | Increase from 0.005 to 0.018 ratio unit after inoculation with *F. culmorum* | [71]      |
| Trichodiene    | Increase from 0.009 to 0.027 ratio unit after inoculation with *F. culmorum* |           |
| (-)β-Chamigrene| Increase from 0.003 to 0.012 ratio unit after inoculation with *F. culmorum* |           |
| (Z)-hex-3-enal | Increase from 14 to 139 ng sample$^{-1}$ after inoculation with *F. graminearum* |           |
| (E)-hex-2-enal | Increase from 1 to 709 ng sample$^{-1}$ after inoculation with *F. graminearum* |           |
| (E)-hex-2-en-1-ol | Increase from 9 to 881 ng sample$^{-1}$ after inoculation with *F. graminearum* | [70]     |
| (Z)-hex-3-en-1-yl acetate | Increase from 22 to 218 ng sample$^{-1}$ after inoculation with *F. graminearum* |           |
| Hex-1-en-1-yl acetate | Increase from 3 to 477 ng sample$^{-1}$ after inoculation with *F. graminearum* |           |

Pp: purple pericarp; Ba: blue aleurone; R: red grain colour; FAE: ferulic acid equivalent; GAE: gallic acid equivalent; RE: retinol equivalent; MR: moderately resistant; R: resistant; S: susceptible; DW: dry weight; DM: dry matter; FW: fresh weigh.

#### 3.1.2. Passive Resistance

Plant morphology can play an important role during infection and provide a passive way of resistance or susceptibility to FHB [72–74]. In general, Steiner et al. [72] and Jones et al. [73] confirm that earlier flowering varieties and taller plant height show greater resistance compared to later flowering and shorter varieties [75–77]. Positive correlations between spike compactness and FHB severity have recently been reported from a study by Giancaspro et al. [76]. Other traits associated with FHB include heading time, degree of anther extrusion, and presence or absence of awns. The extent of anther retention after flowering and FHB severity were shown to be positively correlated with the semi-dwarfing allele *Rht-D1b* [78].

#### 4. Secondary Metabolites

Many naturally occurring secondary metabolites in plants are involved in resistance mechanisms against FHB. The majority of these are phenolic compounds with antioxidant properties. Significantly contained in wheat are phenolic acids (in free, conjugated, and bound forms) [79], flavonoids [80,81], alkylresorcinols [82], benzoxazinoids [83], phytohormones [84], and volatile organic compounds [85].

##### 4.1. Phenolic Compounds/Antioxidants

Constituting a broad spectrum of genetic plant defense mechanisms against pathogens, the accumulation of phenolic compounds has been shown to inhibit in vitro growth and reproduction across a wide array of fungal genera and can help in reducing *Fusarium* trichothecene mycotoxin accumulation in cereal grains [86]. Phenolic compounds are secondary metabolites produced by the phenylpropanoid pathway and are synthesized by plants from the amino acid phenylalanine [87]. Plant biosynthesis produces various phenols that are commonly grouped as phenolic acids and flavonoids.

##### 4.1.1. Phenolic Acids

Phenolic acids are predominant in cereal grain extracts and are derivatives of either cinnamic acid or benzoic acid (Figure 1). In wheat, they include (in descending quantity) ferulic, sinapic, 4-hydroxybenzoic, vanillic, and caffeic acids [67]. Their contents in common wheat are substantially greater as compared with durum wheat (Table 1). This corresponds
to the facts that durum wheat (*Triticum turgidum sp. durum*) is notable for its extreme susceptibility to FHB and that sources of FHB resistance are rare in the gene pool of the tetraploid wheat [77]. Indeed, Stuper-Szablewska and Perkowski [67] found in durum wheat only ferulic, *p*-coumaric, and syringic acids, whereas common wheat contained in addition gallic, 4-hydroxybenzoic, vanillic, chlorogenic, caffeic, and sinapic acids. Phenolic acids can be ranked as follows in ascending order of toxicity toward *F. graminearum*: chlorogenic acid < *p*-hydroxybenzoic acid < caffeic acid < syringic acid < *p*-coumaric acid < ferulic acid [80]. Martin [68] found a weak but significant effect of ferulic acid (FA) on resistance against *Fusarium* according to FA levels in grains but suggests that FA levels in grains are generally low (Table 1). Across all genotypes, however, the FA content increased significantly from 97.1 mg kg\(^{-1}\) in flowering tissues to 120.4 mg kg\(^{-1}\) 10 days after anthesis. The effectiveness of phenolic acids against *Fusarium* spp. could be related to their antioxidant activity, which Verma et al. [66] measured in six wheat cultivars. In their study, high antioxidant activity as determined by ABTS test (using 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) was proven for *trans*-ferulic acid, syringic acid, sinapic acid, and caffeic acid, all of which were obtained by acid hydrolysis. Among the alkaline hydrolyzed phenolic acids, higher antioxidant activity was shown for ferulic acid, *p*-coumaric acid, sinapic acid, and vanillic acid, respectively. Generally, the total content of all phenolic acids may be an important factor in their protective effect against *Fusarium* spp.

**Figure 1.** Structures of phenolic acids in wheat.

Phenolic acids found in cereals exist in both soluble (free) and insoluble (cell wall-bound) forms [88]. For free phenolic acids, 80% ethanol [66,89], methanol/water (80:20, *v*/ *v*) [88,90], or methanol-water (70:30, *v*/ *v*) acidified with 0.1% formic acid is generally used [91]. In addition, different ratios methanol/water are used (7:3, 1:1, *v*/ *v*) [56,92], but also 95% ethanol or dimethyl sulfoxide has been used [93]. Bound or conjugated phenolic acids should be released by alkaline (with 2 M NaOH) and acidic hydrolysis (with 6 M HCl) [56,66,88]. Martini et al. [60] used, for extraction of phenolic acids, ethanol/water
(80:20, v/v) and ethyl acetate, alkaline hydrolysis after initial ethanol/water extraction with 2 m sodium hydroxide, and successive extraction with ethyl acetate.

The major part of phenolic compounds is in the germ and bran tissues of grains. Moreover, phenolic acids, and most predominantly ferulic and p-coumaric acids, have an important role in limiting polysaccharide degradation by exogenous enzymes, where they act as a cross-link between polysaccharides and between polysaccharides and lignin [89]. Phenolic compounds in plants are involved in the pathogen and plant interaction. In wheat (winter and spring cultivars), significantly greater amounts of free phenolic compounds were detected in the glumes, lemmas, and paleas of the spring cultivars prior to and at all sampling times after inoculation compared to the winter wheat cultivars [94]. The spring cultivars show resistance against initial infection by the fungus [94]. Inasmuch as p-coumaric acid increases significantly in the glumes, lemmas, and paleas of the spring cultivars, it appears that phenolic compounds play a role in cultivars’ resistance to F. culmorum. In cereals, cell wall-bound ferulic acid (FA), along with its dehydrodimers, as well as free chlorogenic acid and its hydrolyzed product caffeic acid, could be key components of resistance to toxigenic Fusarium species [95]. In a later study by Schönberg et al. [93], FA had a significant influence on the growth of Fusarium species (F. poae, F. graminearum, and F. langsethiae) in comparison with the control treatment (p < 0.001). In their study, the black oat varieties Gailette and Zorro differed significantly and had as much as two times higher levels of FA compared with the yellow or white varieties Canyon and Husky. Inoculation with F. langsethiae caused reduction relative to the controls (by as much as 96–100% for FA and 97–100% for p-hydroxybenzoic acid). The reduction was complete after F. langsethiae inoculation in the case of vanillic acid across all examined varieties. Despite the overall reduction, the black oat varieties had significantly higher FA levels in comparison with white and yellow-hulled varieties. FA had a significant effect on the growth of all Fusarium species. In the case of F. graminearum, increasing FA concentration significantly decreased fungal growth relative to the control treatment, the reduction ranging from 3% (at 100 µg FA g⁻¹, p > 0.05) to 64% (at 1000 FA µg g⁻¹, p < 0.001) and to 88% (at 5000 µg FA g⁻¹, p < 0.001) [93]. The same trend in reduction was observed for F. langsethiae. In contrast to FA, however, F. poae and F. graminearum exhibited an increase in growth when exposed to p-hydroxybenzoic acid and vanillic acid, whereas F. langsethiae showed mostly a decrease in growth. FA and p-hydroxybenzoic acid showed no significant effect on any mycotoxin, whereas quercetin had a minor but significant decreasing effect on neosolaniol and diace

white and yellow-hulled varieties. FA had a significant effect on the growth of all cultivars relative to the control treatment, the reduction ranging from 3% (at 100 µg FA g⁻¹, p > 0.05) to 64% (at 1000 FA µg g⁻¹, p < 0.001) and to 88% (at 5000 µg FA g⁻¹, p < 0.001) [93]. The same trend in reduction was observed for F. langsethiae. In contrast to FA, however, F. poae and F. graminearum exhibited an increase in growth when exposed to p-hydroxybenzoic acid and vanillic acid, whereas F. langsethiae showed mostly a decrease in growth. FA and p-hydroxybenzoic acid showed no significant effect on any mycotoxin, whereas quercetin had a minor but significant decreasing effect on neosolaniol and diacetoxyscirpenol. Giordano et al. [96] observed a significant negative correlation between DON contamination in corn (Zea mays L.) at harvest maturity and free phenolic acids and total antioxidant activity at the beginning of kernel development, whereas no significant correlation was observed with fumonisins contamination. Ferulic, p-coumaric, and caffeic acids were the main cell wall-bound phenolic acids during kernel development, whereas chlorogenic acid was the main free phenolic acid. In a study of fungal biotransformation of chlorogenic acid with F. graminearum, Gauthier et al. [95] demonstrated that F. graminearum possesses the ability to degrade chlorogenic acid into caffeic, hydroxychlocogenic, and protocatechuic acids, as well as caffeic acid into protocatechuic and hydroxycaffeic acids. Some of these metabolic products can contribute to the inhibitory efficiency of chlorogenic acid, thereby corroborating the contribution of chlorogenic acid to the chemical defense that cereals employ to counteract F. graminearum and its production of mycotoxins. Among the phenolic acids, derivatives of cinnamic acid, such as caffeic, ferulic, and p-coumaric acids, are most recognized as contributors to FHB resistance [91,95]. Cinnamic acid derivatives also have strong antioxidant properties, which constitute an important primary factor for the ability of phenolic acids to modulate mycotoxin production [95]. Similarly, in corn, the most efficient resistance factors were shown to be pericarp propanoids, mainly trans-ferulic acid, cis-ferulic acid, p-coumaric acid, and diferulates [97].

Another phenolic acid, salicylic acid, plays a significant role in plant immunity as a signaling molecule in eliciting resistance and increases its activity during the early phase of infection by F. graminearum [98,99]. In a recent study, Rocheleau et al. [99] reported that
F. graminearum could utilize salicylic acid as a sole source of carbon to grow. Salicylate 1-monoxygenase and catechol 1,2-dioxygenase are two of the first key enzyme steps for salicylate degradation via catechol in the β-oxoadipate pathway. There also exists, however, a nonoxidative decarboxylation pathway of salicylic acid conversion to catechol via 2,3-dihydroxybenzoic acid [99].

Deoxynivalenol (DON) accumulation is enhanced by peroxide stress [92], and the inhibition of its production by phenolic acids is consistent with their ability to scavenge reactive oxygen radicals [91]. Nevertheless, there exist differences between strains of F. graminearum and F. culmorum carrying the DON chemotype, where enhancement of deoxynivalenol and acetyldeoxynivalenol production was recorded, and those strains carrying the nivalenol chemotype, wherein the same treatment yielded a 2.4- to 7-fold decrease in nivalenol and fusarenone accumulation [100,101]. There should be further investigation of interactions between different phenolic compounds that frequently co-occur in cereal grains [93].

4.1.2. Anthocyanins and Flavonoids

Flavones, flavonols, flavanones, flavan-3-ols, anthocyanidins, isoflavones, coumarins, stilbenes, and lignans are the main flavonoids and have various functions, including pigmentation and resistance to pathogens in plants [102,103]. The abundance and composition of these compounds in cereal grains contribute to either constitutive or induced synthesis and are highly variable depending upon the species, cultivar, and environmental conditions (Figure 2). Many phenolic compounds are bound to the cell wall, indicating that they are parts of the preformed general defense system against potential pathogens [104]. The specific biochemical pathways and mechanisms of their antifungal activity are not yet fully understood, however. Flavonoids comprise another group of compounds with antioxidant activity and have been identified from many plants. Some of them suppress trichothecene biosynthesis [49,52,93]. Anthocyanins have a protective role under conditions of extreme temperature, drought, and/or salinity, as they prevent lipid oxidation and protect the plasma membrane from damage [105]. Because infection of plants by various pathogens is accompanied by oxidative stress, the presence of anthocyanins in a plant may have a positive effect on the resistance to abiotic stress [106].

Anthocyanins in a plant are extracted with acidified methanol with HCl-methanol/hydrochloric acid (85:15, v/v) [68,107], flavonoid aglycones [90] with 96% ethanol [9], for flavonoid glycosides methanol and acetonitrile are eluents, followed by alkaline hydrolysis (water/2 M NaOH, 1:4, v/v) [9,64] and acid hydrolysis (6 M HCl) and diethyl ether. Additionally, dimethyl sulfoxide (DMSO, 0.5–100 μM) can be used [102]. Several anthocyanins were identified by NMR spectroscopy and mass spectrometry after sequential extraction of blue bread wheat ‘UC66049’ with solvents of various polarities and multiple chromatographic fractionations [108].
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4.1.2. Anthocyanins and Flavonoids

Flavones, flavonols, flavanones, flavan-3-ols, anthocyanidins, isoflavones, coumarins, and lignans are the main flavonoids and have various functions, including pigmentation and resistance to pathogens in plants [102,103]. The abundance and composition of flavonoids can interfere with mycotoxin production. The antioxidative properties of phenolic acids and flavonoids may apply here. In fact, FA was shown to contain large amounts of FA and vanillic acid [93,111]. It is Nevertheless likely that the fungus metabolized an extensive amount of the endogenous phenolic compounds, thereby leading to the observed differences between control and inoculated treatments. This was reported also by Bilska et al. [9]. In their study, trichothecene accumulation by F. culmorum and F. graminearum was significantly reduced by quercetin, kaempferol, luteolin, apigenin, and naringenin, although this effect was dependent upon the fungal strain and flavonoid levels (Figure 3). Nevertheless, correlation between antiradical and antioxidant properties of flavonoids and their effect on Fusaria was established. Antioxidant properties of flavonoids such as quercetin can interfere with mycotoxin production, but FA is considered the most potent phenolic acid with antifungal activity against Fusarium species [80]. It is clear that the antioxidant properties of phenolic acids and flavonoids apply here. In fact, the most consistent overall inhibition of mycelial growth was observed with FA treatments. Nevertheless, impacts of naringenin, apigenin, kaempferol, and quercetin at concentrations 400 mg kg⁻¹ and 800 mg kg⁻¹ in inhibiting mycotoxin accumulation were also reported [9].

The flavanone naringenin with a single bond between C2 and C3 was more efficient than apigenin, having a double bond between these two carbon atoms. In a study by Bollina and Kushalappa [112], naringenin at LD₅₀ concentration 1.58 mM and quercetin at LD₅₀ concentration 2.95 mM totally inhibited biosynthesis of DON and 3-acetyldeoxynivalenol in barley, as similarly did p-coumaric, sinapic, ferulic, and caffeic acids, respectively, at LD₅₀ concentrations 1.15, 1.74, 1.76, and 2.50 mM. Levels of apigenin, kaempferol, luteolin, naringenin, quercetin, rutin, and vitexin were significantly increased in winter wheat after inoculation with Fusarium culmorum [64] (Table 1). Gunnaiah and Kushalappa [113] found that in resistant wheat cultivars, accumulation of such phenylpropanoids as syringyl-rich monolignols and their glucosides reduced pathogen colonization and increased wheat cell wall thickening. They considered phenylpropanoid pathway genes responsible for

| Aglycone    | R₁   | R₂   | R₃   |
|-------------|------|------|------|
| Delphinidin | OH    | OH   | OH   |
| Cyanidin    | OH    | H    | OH   |
| Petunidin   | OCH₃  | OH   | OH   |
| Peonidin    | OCH₃  | H    | OH   |
| Malvidin    | OCH₃  | OCH₃ | OH   |
| Pelargonidin| H     | H    | OH   |

Figure 2. Structure of anthocyanins identified in wheat grains.
flavonoid biosynthesis to have enhanced host resistance mechanisms and reduced pathogen growth due to the antifungal and antioxidant properties of biosynthesized flavonoids and lignols [113] (Figure 3).

![Flavonoids and Monolignols](image)

**Figure 3.** Structure of (a) aglycones of flavonoids and (b) monolignols determined in wheat grains.

Lignans have been discovered in different parts of plants, including seeds [114]. These are vascular plant secondary metabolites, which are attributed for a wide range of physiological functions and beneficial properties [115]. Pathogen attack may accelerate the rate of lignin and lignans synthesis and deposition, which results in an inhibition of pathogen growth and its confinement [116].

4.1.3. Alkylresorcinols

Alkylresorcinols (AR), also known as resorcinolic lipids, are phenolic lipids composed of long aliphatic chains and resorcinol-type phenolic rings (Figure 4). Alkylresorcinols are relatively rare in nature, with the main known sources being wheat, rye, barley, and triticale (i.e., cereal grasses). Alkylresorcinols are present in large amounts in the bran layer (e.g., pericarp, testa, and aleurone layers) of wheat and rye (0.1–0.3% of dry weight) [117]. Alkylresorcinols can also be found in rice, though not in the edible parts of the rice plant [118]. They are present in the endosperm (the part of cereal grain used to make white flour) only in exceptionally low amounts, which means that alkylresorcinols can be used as biomarkers for people who eat foods containing wholegrain wheat and rye rather than cereal products based upon white flour [54,119]. Similarly, in a study by Ziegler et al. [53] bread wheat (761 ± 92 mg g⁻¹ DM) and spelt (743 ± 57 mg g⁻¹) belonging to the hexaploid species showed higher AR levels than did the tetraploid durum (654 ± 48 mg g⁻¹, p < 0.05), while the levels found in the diploid einkorn (737 ± 91 mg g⁻¹) and the tetraploid emmer (697 ± 94 mg g⁻¹) did not differ significantly from those in the other species.

![5-n-Alkylresorcinols](image)

**Figure 4.** Structure of 5-n-Alkylresorcinols identified in wheat grains: 5-n-heptadecylresorcinol (C17:0), 5-n-nonadecylresorcinol (C19:0), 5-n-heneicosylresorcinol (C21:0), 5-n-tricosylresorcinol (C23:0), 5-pentacosylresorcinol (C25:0).
Alkylresorcinols are extracted by acetone, methanol, or mixture methanol/methyl-tert. butyl ether (MeOH/MTBE, 1:1, v/v), ethyl acetate or n-hexane [53]. Landberg [54] used diethyl ether and methanol, while Suzuki et al. [118] used 10% MeOH/CHCl₃.

Righetti et al. [56] have suggested involvement of the lipophilic phenolic fraction in mycotoxin accumulation in wheat. The contamination, expressed as the sum of DON and deoxynivalenol 3-glucoside, was found to be significantly lower in common wheat and spelt than in emmer, durum wheat, and einkorn, while following the trend hexaploid < tetraploid < diploid species. The mycotoxins content negatively correlated with the total 5-n-alkylresorcinols, and the AR21:0/AR23:0 ratio (AR21:0 is 5-n-heneicosylresorcinol, where the saturated hydrocarbon chain attached to position 5 of resorcinol consists of 21 carbon atoms; AR23:0 is 5-n-tricosylresorcinol having 23 carbon atoms and no double bonds, Figure 4) was recently reported by Righetti et al. [56] as an indicator of antifungal activity. Their results suggest that only the lipophilic phenolic fraction in wheat exerts an inhibitory effect on mycotoxin accumulation [56].

4.2. Benzoxazinoids

The principal phytoanticipin in wheat and corn is 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA, Figure 5). For the extraction of benzoxazinoids, 70% methanol coupled with accelerated extraction system is generally used, as it is described by Kowalska and Kowalczyk [120]. DIMBOA accumulation is regulated by jasmonic acid in both the aboveground parts of wheat and the roots [121]. A recent study found that jasmonic acid signaling and DON detoxification have relevance for seedling resistance and that seedling development and root growth are jasmonic acid-controlled processes [122]. The results of this study confirm that development-specific determinants of resistance against Fusarium are more significant than are the organ-specific determinants, and suggest roots to be an important organ in studies of Fusarium–wheat interactions.

![Structure of 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA)](image)

Figure 5. Structure of 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA) detected in wheat grains.

4.3. Volatile Organic Compounds

Pathogen infestation of vegetative tissues can induce volatile organic compounds (VOCs) production, which can in turn provide defensive functions to both injured and uninjured plants. In wheat, oats, and barley, the blend of VOCs induced after Fusarium spp. infestation was dominated by (Z)-hex-3-enal, (E)-hex-2-enal, (E)-hex-2-en-1-ol, (Z)-hex-3-enyl acetate, 1-hex-1-enyl acetate, β-linalool, and β-caryophyllene [70] (Figure 6). Buško et al. [71] recently reported findings about VOCs contained in the grain of winter wheat varieties under controlled conditions after inoculation with F. culmorum. Among hydrocarbons, alcohols, aldehydes, ketones, aromatics, terpenes, and other components, terpenes were of particular importance [71] (Figure 6). Interestingly, the terpenes produced in wheat grains were further changed by F. culmorum into other compounds that were more toxic. Significantly large quantities of terpenes were observed in wheat grains inoculated with F. culmorum compared to uninoculated control samples. Trichodiene, thujopsene, and β-chamigrene were dominant in inoculated samples, while α-pinene, indane, and 3-carene dominated in control samples.
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![Figure 6. Structure of (a) terpenes and (b) volatile organic compounds determined in wheat grains.](image)

Nazareth et al. [123] used the volatile gaseous fumigant allyl isothiocyanate that is not contained in wheat (an antimicrobial organosulfur compound that can be obtained from mustard *Brassica* spp.) to restrict the production of beauvericin and enniatin produced by *Fusarium poae* in wheat flour. Synthesis of beauvericin was more inhibited than was that of enniatin.

4.4. Phytohormones

When studying the influence of phytohormones on the defense response of wheat against *F. graminearum* infection, Qi et al. [69] determined that infection of heads with *F. graminearum* induced accumulation of salicylic acid, jasmonic acid, abscisic acid, and indole acetic acid [69] (Figure 7). Small et al. [124] and Trapp et al. [125] reported the extraction of these phytohormones can be provided with methanol, ethyl acetate, mixture acetone-ethanol-water (1:1:2, v/v/v) or 100% cold methanol, dichlormethane, or isopropanol, respectively. Jasmonic acid treatment reduced *F. graminearum* growth and FHB symptoms even as an increase in FHB was observed with abscisic acid [69]. After the application of some elicitors, including methyl jasmonate, on *Fusarium verticillioides* in corn, however, Small et al. [124] determined that these were not effective for reducing Fusarium ear rot and fumonisim contamination.
The carotenoids are yellow pigments with antioxidant and photoprotective properties that belong to the terpenes, and their basic structure consists of eight isoprene units. Two classes of carotenoids can be distinguished: (1) carotenes are pure hydrocarbons, and (2) xanthophylls are derivatives containing one or more oxygen atoms. A wide range of carotenoids may be present in wheat grain, including lutein, β-carotene, β-cryptoxanthin, zeaxanthin, antheraxanthin, taraxanthin (lutein 5,6-epoxide), tritocoxanthin, and flavoxanthin [51] (Figure 8). Carotenoids are efficiently extracted with mixture ethanol/acetone/hexane (1:1:2, v/v/v) [126]. In another study, extraction with hexane/ethyl acetate mixture (9:1, v/v) after incubation with KOH, 95% ethanol, NaCl (10 g L\(^{-1}\)) and pyrogallol (60 g L\(^{-1}\) ethanol) has been applied [127]. Lutein is the most abundant carotenoid, followed by zeaxanthin, antheraxanthin, α-carotene, and β-carotene, while β-cryptoxanthin is a minor component or it occurs at non-detectable levels [51,126].

Bread wheat (Triticum aestivum L.) is poor in carotenoids, but durum wheat (Triticum durum Desf.) and other related species, such as einkorn (T. monococcum L.), showed higher carotenoid content and thereby potential as donors of useful traits [128]. Carotenoid content and color are influenced by intrinsic genotypic characteristics [51,129], and to a lesser extent by environmental conditions [62]. Delgado et al. [127] observed durum wheat cultivars to show greater lutein content than did common wheat cultivars. In their study, durum wheat was more susceptible to mycotoxin contamination than was common wheat. Positive correlations between the levels of lutein and mycotoxins in durum wheat cultivars were detected for the following mycotoxins: DON and its derivative DON-3-glucoside, moniliformin, as well as culmorin and its derivatives [127]. Martini et al. [60] observed stronger impact of genetic factors on the content of yellow (carotenoid) components and total antioxidant capacity in durum wheat, while content of total polyphenolics and phenolic acids was mostly affected by environmental conditions.

In wheat genotypes with higher levels of FHB resistance, the individual metabolites involved with particular efficiency in protection processes are represented in various proportions and they all contribute to final resistance. The degree of a particular genotype’s resistance will depend upon its genetic and enzymatic equipment for biosynthesis of the active metabolites and corresponds to the content of these compounds in the grain. Therefore, the representation of compounds with resistance activity in each genotype should be comprehensively determined and assessed.

Figure 7. Structure of phytohormones determined in wheat grains.

4.5. Carotenoids
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Figure 8. Structures of carotenoids determined in wheat grains.

5. Pigmentation of Grains and FHB Resistance

The host deploys distinctive resistance mechanisms in different organs of wheat against *F. graminearum* [130,131]. Grain color and its relationship to resistance is the aspect most intensively studied. There exists various coloration of the grain in wheat due to levels of biologically active pigments possessing antioxidant capacity [51]. Descriptions of grain color in wheat are generally qualitative in nature: white, yellow, red, blue, or purple. Red pigmentation is associated with deposition of proanthocyanidins in the testa, whereas both blue and purple pigmentations derive from the accumulation of anthocyanins in the aleurone and the pericarp [132,133].

Anthocyanins can be synthesized in wheat genotypes in grains and in various organs, and they can be involved in the plant response to oxidative stress. Anthocyanins can be contained in the pericarp (purple coloration) or aleurone (blue coloration). When they are contained in both tissues, the color of the grains turns to a dark brown–black shade [134]. Hexaploid wheat varieties are being bred today with increased carotenoid content in the grain, and especially with higher lutein content. The highest carotenoid contents have been observed in yellow- and purple-grained genotypes [126].
In addition to the yellow grain color shades occurring due to carotenoids content, wheat varieties also exist that contain anthocyanins in the aleurone or pericarp layers causing blue and purple grain coloring [135].

6. Use of Antioxidants in Breeding for FHB Resistance

The best strategy for controlling FHB is to breed new varieties with reduced susceptibility. Colored-grain wheats are a potentially great alimentary source of other health-enhancing compounds, such as anthocyanins [51,136], tocols [137], and phenolic acids [88]. Expanding the breeding interest in the use of wheat forms with different grain color and plant organs can be a potential benefit for the creation of lines with increased resistance to various stresses. Spanić et al. [138] have demonstrated that differences in the antioxidant response of wheat varieties can be a valuable marker for the selection of FHB resistance. Rapid activation of the antioxidant system appears to be important in overcoming FHB, but the timing and type of antioxidant enzymes expressed are important. A large amount of variability in enzyme activity and H$_2$O$_2$ content exists within wheat varieties [138]. Measurements of ROS levels and the scavenging activities of antioxidant contents may be very useful for breeding programs to screen and select FHB-resistant varieties [41].

An example of a variety in which secondary metabolites have been implicated in FHB resistance is the most commonly used source of breeding material for FHB resistance, the cultivar Sumai 3 [113]. Gunnaiah and Kushalappa [113] report that several resistance-related metabolites produced in Sumai-3 can explain several mechanisms of resistance. Resistance in the Sumai-3 cultivar to FHB is mainly due to phenylpropanoid and flavonoid metabolites. Antimicrobial compounds and cell wall thickening by hydroxycinnamic acid amides in Sumai-3 also resist FHB [113].

Results obtained by Etzerodt et al. [49] could form a basis for choosing wheat cultivars using metabolite profiling as a marker for selecting wheat cultivars with improved resistance against FHB and accumulation of trichothecene toxins in wheat heads. They found that several phenolic acids, lutein, and β-carotene affected DON accumulation, but the effect varied for the two studied wheat types (spring versus winter wheat).

Furthermore, positive experiences in examining crops other than wheat have also been reported. In corn silk and kernels, induced expression of 3-deoxyanthocyanidins and flavan-4-ols imparted resistance to *F. verticillioides* and *F. graminearum* [40]. Expression data revealed that flavonoid pathway *P1* and *P2* genes were active during the early stages of silk development and *PR-4* and *PR-5* genes showed developmental and fungus-induced expression [40]. Anthocyanins can contribute to antioxidant properties of the polyphenolic complex, but they are unstable and can be easily degraded. Thus, their effects on fungi are not yet entirely clear. In their study of *F. graminearum* effect on wheat genotypes, Martin et al. [139] found no relationship with anthocyanin levels, which were affected more by environmental conditions. Meanwhile, Bernardi et al. [140] determined the red corn cultivar Rostrato Rosso having the greatest accumulation of anthocyanins to be highly resistant to the penetration and diffusion of *F. verticillioides*. Similarly, in a study by Lorenz-Kukula et al. [141], expression of specific genes in flax increased resistance against *Fusarium* and resulted in a significant increase in the levels of anthocyanins and flavonoids and in their antioxidant capacity. In addition, metabolomic analysis of a red cotton mutant (S156) resistant to *Verticillium dahliae* showed enrichment of flavonoids and anthocyanins and upregulated expression of flavonoid biosynthesis genes [142].

On the other hand, it is known that there also exists varieties with colored grains that show susceptibility to FHB. An example is the variety Skorpion with blue grain. Although the anthocyanins which it contains are considered to offer health benefits due to their antioxidant effects, the variety shows susceptibility to FHB [90]. Thus, grain color alone cannot be taken as a marker to detect resistance. Moreover, for varieties with colored grain, it is always necessary to evaluate varietal resistance in trials through artificial infection.
7. Conclusions and Future Directions

In conclusion, many compounds like hydrophilic and lipophilic antioxidants (phenolic compounds such as phenolic acids, anthocyanins, flavonoids, and lipophilic carotenoids), alkylresorcinols, volatile organic compounds, phytohormones, and benzoxazinoids can be involved in protective mechanisms against FHB, the most common disease affecting wheat. However, these protective compounds affect Fusarium strains in varying degrees depending upon their antioxidant activity and different biochemical and cellular mechanisms. Complete resistance to F. graminearum is not detected in any host plant, and selection of FHB-resistant genotypes remains challenging. Therefore, considerable effort is needed to gain more in-depth insight into the genetics of the pathogen populations and to find novel and effective resistance markers in various hosts, as well as to identify the major components of cereals’ defense against the pathogen. It follows that more detailed studies are required to obtain a better understanding of the protective effects and modes of activity of these metabolites. Indirect selection for an antioxidant response associated with FHB resistance can be performed and the antioxidative mechanism plays a significant role against Fusarium biotic stress in wheat and other cereals. The efficient use of native resistance in the wheat gene pool, introgression of resistant alleles, and implementation of modern genotypic strategies to increase levels of native secondary metabolites with antifungal properties can enhance FHB resistance of new wheat varieties. A complex of secondary metabolites composed of individual antioxidants and compounds having antifungal efficiency, with their various contents and possible synergistic effects, can determine the resistance of wheat genotypes. In short, more detailed studies are warranted concerning new wheat genotypes, their native resistance metabolites, and the effects of these upon FHB.

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