**Natural Product-Based Resistance in Wheat to Aphid Virus Vectors: Progress and Future Opportunities**

**Running title:** Natural Product-Based Resistance against *Sitobion* *avenae* and *Rhopalosiphum padi* in wheat.

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**Abstract**

Cereal aphids, *Sitobion avenae* and *Rhopalosiphum padi*, cause severe yield loss in wheat crops as a consequence of direct feeding damage and acting as vectors for Barley Yellow Dwarf Virus (BYDV). Insecticides have commonly been used to control these pests, however, the advent of insecticide resistance spreading across aphid populations and the push to reduce insecticide use means that new approaches to control aphid populations are required. Wheat varieties with natural product-based aphid resistance have been identified, suggesting that they could be developed as an alternative to insecticides. Resistance induced by natural products include volatile organic compound-mediated (antixenotic) and development-modifying (antibiotic) processes. Full characterisation of these resistance mechanisms is still required, and associated challenges, such as the influence of biotic and abiotic interactions, need to be addressed prior to their implementation into integrated pest management (IPM) or engineered into modern elite wheats. In this review, current literature on natural product-based *S. avenae* and *R.padi* resistance in wheat is discussed, outlining current knowledge gaps and challenges and highlighting future work required.

**Keywords:** Aphid resistance, Natural products, Primary metabolites, *Rhopalosiphum padi,* *Sitobion avenae*, Wheat, Triticum.

1. **Introduction**

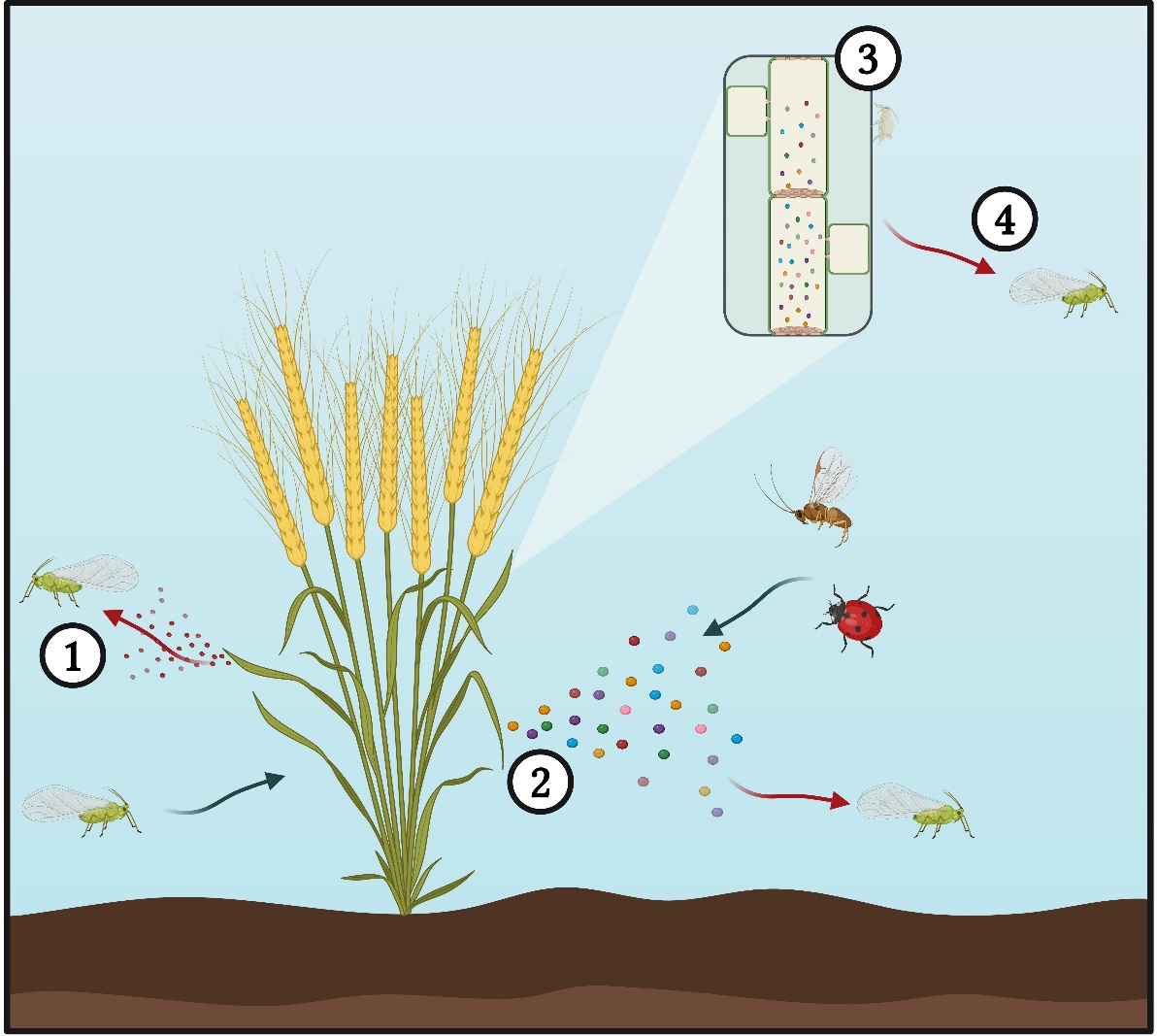
Wheat, *Triticum aestivum* L. (Poaceae), is a globally important staple food crop (FAO(https://www.fao.org/faostat). Aphids (Hemiptera: Aphididae) are the most economically important pest insects on wheat,1 causing damage either by phloem-feeding or virus transmission.2 Phloem-feeding by cereal aphids reduces nutrient availability for the plant.3 Saprophytic fungal growth on aphid honeydew also lowers photosynthesis efficiency.4 Virus transmission, such as the spread of the Barley Yellow Dwarf Virus (BYDV), can lead to wheat yield losses of up to 80% .1

Currently, control of aphid infestations is mainly achieved through deployment of broad-spectrum insecticides.1 However, insecticide use is jeopardised due to increasing incidences of insecticide resistance across aphid populations and banning of insecticides, e.g. across the European Union, due to their environmental impacts.5,6 This has reduced options that farmers have available to manage pest aphids and highlights the need to identify new approaches to control infestations. New approaches include the use of soil additives,7 incorporation of integrated pest management strategies tailored to aphids,8 and use of transgenic plants.9,10 In this review, we focus on the development of naturally-occurring aphid resistance across modern and ancestral wheat lines, which can be engineered into modern elite wheat cultivars, an approach successfully developed against the Russian wheat aphid, *Diuraphis noxia* (Kurdjumov).11

Whilst naturally-occurring aphid resistance in wheat can include both physical barriers and natural product-based mechanisms,12 this review focuses on the latter modes of resistance. Wheat aphid resistance can be conferred through the release of volatile organic compounds (VOCs) that modify aphid host-seeking behaviour (antixenosis) or through the presence of non-volatile primary and secondary metabolites present in the leaves, phloem and roots that modify aphid feeding or development (antibiosis) (Figure 1). In general, primary metabolites confer resistance by providing reduced amounts of nutrients for aphid development, whilst secondary metabolites act as antifeedants or short-range deterrents. Secondary metabolites can be constitutively produced, or induced by hormonal signalling in response to aphid feeding.12 Although classification of metabolites as primary and secondary metabolites is a debated topic,13 this nomenclature is used throughout this review.

English grain aphids, *Sitobion avenae* (Fabricius), and bird cherry-oat aphids, *Rhopalosiphum padi* (L.)*,* are the main pest aphids of cereals across the UK and northern Europe, also affecting other major wheat-growing regions such as South America and China.1,14 Both species are vectors for BYDV, which causes yield losses of 5-80%, making it one of the most economically important aphid-vectored cereal viruses globally.1 The use of insecticides to control aphid populations in turn limits the spread of BYDV which often causes higher yield losses than direct aphid damage.15 However, the development of insecticide resistance across aphid populations reduces the efficiency to control against BYDV. Insecticide resistance monitoring across aphid populations has therefore increased in recent years to determine the efficacy of insecticide use in controlling cereal aphids, and in turn BYDV. From across 30 and 29 *S. avenae* and *R. padi* populations monitored in China, respectively, two *S. avenae* and four *R. padi* populations showed high pyrethroid resistance, whilst all populations showed low to moderate neonicotinoid resistance.16 Genotypic screening of *S. avenae* populations across Ireland and the UK found the moderately pyrethroid-resistant SA3 super clone containing the ‘knockdown resistance’ (*kdr*) mutation was dominant in both countries between 2016-2018.6 Further screening in the UK across 2019-2020 showed moderate pyrethroid resistance in *S. avenae* populations was maintained; however, no signs of resistance was observed in *R. padi*.17 The first case of *S. avenae* with the *kdr* mutant providing pyrethroid resistance was identified in northern France in 2021.18 More recently, three of 25 sampled *S. avenae* populations from Lower Saxony, Germany, showed similar levels of pyrethroid resistance to *kdr* mutants and the first instance of reduced pyrethroid sensitivity in Germany for *R. padi*.19 Current aphid control measures via insecticide use remains effective; however, increased selective pressures induced by pyrethroids following the ban of neonicotinoids in the UK and EU indicates that continual screening for pyrethroid resistance across aphid populations is important to maintain effective aphid control.17,19 This also highlights the need to identify alternative aphid and associated virus control measures.

**Figure 1** Natural product-based aphid resistance mechanisms observed across wheat. 1: Constitutively produced volatile organic compounds (VOCs) induce antixenosis towards aphids. 2: Aphid-induced VOCs induce antixenosis towards aphids and attraction towards aphid natural enemies. 3: Constitutive or aphid-induced phloem metabolites induce toxicity towards aphids upon feeding (antibiosis). 4: Constitutive or aphid-induced phloem metabolites deter aphids from establishment on host plant (antibiosis). Green arrows = attraction, red arrows = repellence. Created in BioRender. Birkett, M. (2024) BioRender.com/z52z425.



Modern elite wheat varieties with BYDV resistance, such as RGT Wolverine, RGT Grouse and MN-Washburn, has been developed in recent years, conferring resistance via the *‘bdv2’* gene originating from *Thinopyrum intermedium* (Barkworth & D.R. Dewey).20–22 It works via pathogen-associated molecular pattern-triggered immunity and may involve viral movement restriction in the phloem and increased phenolic compound production.23,24 Here, we summarise and discuss the current literature surrounding natural product-based antixenotic and antibiotic aphid resistance mechanisms of wheat against *S. avenae* and *R. padi*. Current knowledge gaps, obstacles and research required to develop aphid-resistant modern elite wheat are also highlighted.

1. **Volatile organic compound (VOC)-mediated aphid resistance in wheat (antixenosis)**

*VOC-mediated aphid resistance in modern and ancestor wheat*

Aphid host location, as for other pest-host interactions, is mediated by a number of factors, including olfactory (antennal) perception of VOCs produced and emitted by host plants.25 Constitutively produced VOCs are typically involved in initial host location and colonisation, suggesting the presence of a suitable host for feeding, whilst herbivore-induced plant volatiles (HIPVs) released upon aphid feeding typically result in antixenosis (repellence) of other incoming aphids away from plants, indicating the presence of an unsuitable host due to competition for plant nutrients / overcrowding.26

A number of studies have confirmed the role of hexaploid wheat VOCs in cereal aphid host location. Behavioural (four-arm olfactometry) studies confirmed preference of *R. padi* apterae for a blend of (*Z*)-3-hexenyl acetate, (*E*)-2-hexenyl acetate, (*E*)-2-hexen-1-ol, (*Z*)-2-hexen-1-ol, heptanal, octanal, nonanal, decanal, benzaldehyde and linalool, identified from *T. aestivum* cv. Ciko, and preference of *R. padi* alatae for a blend of (*E*)-2-hexenyl acetate, (*Z*)-3-hexen-1-ol, (*E*)-2-hexen-1-ol and benzaldehyde.27 When tested individually, (*E*)-2-hexenal, (*E*)-2-hexen-1-ol and (*E*)-3-hexenyl acetate elicited the same preference.28 Interestingly, a similar study assaying the behavioural response of *S. avenae* against (*E*)-3-hexenyl acetate, (*Z*)-3-hexen-1-ol and 1-hexanol, when tested individually, showed that increasing concentrations of 1-hexanol caused increased preference, whilst decreased preference occurred with increasing concentrations of (*E*)-3-hexenyl acetate and (*Z*)-3-hexen-1-ol.29 Increasing concentrations of all three compounds was accompanied by a stronger preferential response in the aphid predator, the Harlequin ladybird, *Harmonia axyridis* (Pallas), whilst (*Z*)-3-hexenyl acetate induced preference in another aphid predator, the hoverfly, *Episyrphus balteatus* (De Geer).29 Schröder *et al.* (2015) identified (*Z*)-3-hexenyl acetate as an attractant from multiple maize (*Zea mays* (L.)) and wheat cultivars; however, only *Z. mays* cultivar 6Q-121 induced preference in *R. padi*. Schröder *et al.* (2015) suggested that antixenotic, i.e. repellent, compounds, such as (*E*,*E*)-α-farnesene, indole and (*E*)-2-hexenal, counteract the preference induced by (*Z*)-3-hexenyl acetate in non-attractive cultivars. These studies show several compounds are common across cereals (Table 1), such as (*Z*)-3-hexenyl acetate, and VOC blend composition plays an important role in activity towards aphids, as previously described in the *Aphis fabae* (Scopoli)*–Vicia faba* (L.) aphid-host system by Webster et al. (2010). Aphid species and morphs react to different components within the same VOC blend, highlighting the complexity behind VOC-mediated aphid-host interactions, which needs to be taken into account when used in integrated pest management (IPM) strategies.

**Table 1** Summary of common wheat natural products involved in interactions against Sitobion avenae and Rhopalosiphum padi, identified from at least two wheat accessions. X represents interaction with species.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Compound | Wheat species | Target aphid species | | | Interaction effect compared to controls | Reference |
| ***Rhopalosiphum padi*** | ***Sitobion avenae*** | |
| Volatile organic compounds (VOCs) | | | | | | |
| (Z)-3-Hexenyl acetate | *Triticum aestivum* | **X** | | **X** | Increased attraction | 27, 30, 32 |
| 6-Methyl-5-hepten-2-one | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 28, 33, 34, 35 |
| 6-Methyl-5-hepten-2-ol | *Triticum aestivum* | **X** | | **X** | Decreased attraction | 28, 33, 34 |
| Linalool | *Triticum aestivum*  *Triticum monococcum* | **X** | |  | Increased and decreased attraction | 27, 36 |
| (E)-2-Hexen-1-ol | *Triticum aestivum* | **X** | | **X** | Increased attraction | 27, 28 |
| (E)-2-Hexenal | *Triticum aestivum* | **X** | | **X** | Increased and decreased attraction | 28, 30 |
| Heptanal | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 36, 35 |
| Octanal | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 36, 35, 37 |
| Nonanal | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 35, 32, 37 |
| Decanal | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 36, 35, 32 |
| Hexadecane | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 35 |
| Heptadecane | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 35 |
| Undecane | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 35, 32 |
| Benzaldehyde | *Triticum aestivum*  *Triticum monococcum* | **X** | | **X** | Increased and decreased attraction | 27, 35, 37 |
| Leaf secondary metabolites | | | | | | |
| HDMBOA-glucoside | *Triticum aestivum*  *Triticum durum*  *Aegilops speltoides* | **X** | | **X** | Deterrent | 38, 39, 40 |
| DIMBOA | *Triticum aestivum*  *Triticum durum*  *Aegilops speltoides* | **X** | | **X** | Deterrent | 41, 42, 43, 38, 39, 40 |
| DIMBOA-glucoside | *Triticum aestivum*  *Triticum durum*  *Aegilops speltoides* | **X** | | **X** | Deterrent | 44, 41, 38, 39, 40 |

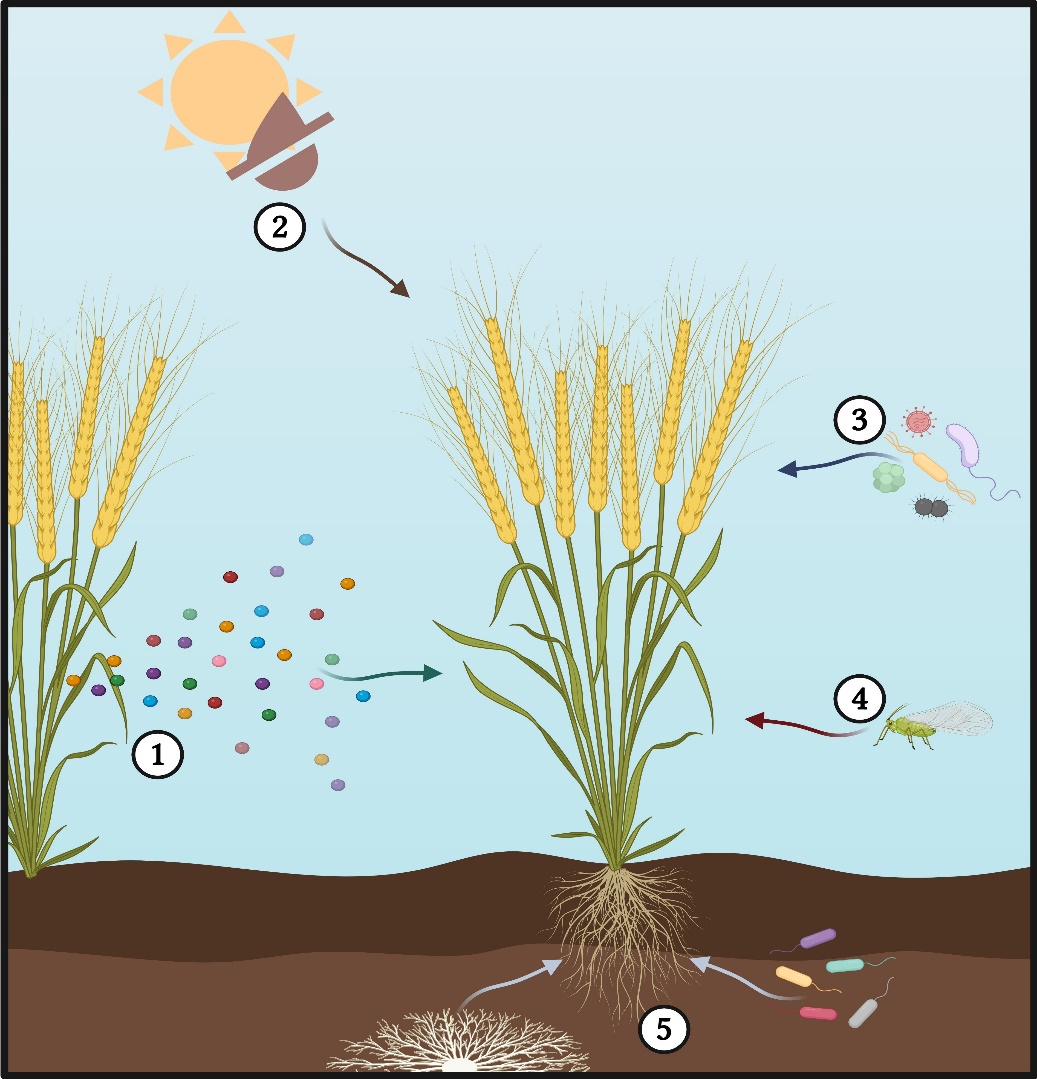
High aphid density on wheat and other cereals increases *R. padi* sensitivity to disturbance, reducing aphid preference,45 with 6-methyl-5-hepten-2-one, 6-methyl-5-hepten-2-ol and 2-tridecanone being responsible for this activity.33 These compounds are thought to originate from the aphids, preventing overcrowding on the host plant (Quiroz *et al.*, 1997) and showed promise for aphid population control in the field on barley (*Hordeum vulgare* L.).33,46 Interestingly, 6-methyl-5-hepten-2-one and 6-methyl-5-hepten-2-ol are HIPVs from the aphid-resistant *T. aestivum* Beijing837, which induce preference in the aphid parasitoid *Aphidius avenae* (Haliday).47 Additionally, saliva-treated *T. aestivum* Beijing837 induced repellent activity against *S. avenae*, but whether 6-methyl-5-hepten-2-one and 6-methyl-5-hepten-2-ol are involved in this activity requires confirmation.34

Whilst VOC-mediated resistance in hexaploid wheat has been reported,34,48 by contrast, for ancestor tetraploid and diploid wheat, studies directly investigating VOC-mediated aphid resistance mechanisms are lacking. However, screening tests mentioned later indicate the presence of potential antixenotic resistance. For example, Liu *et al.* (2022) in choice assays identified *T. turgidum* Lanmai to be less preferred compared to *T. turgidum* Polan305 by *S. avenae,* indicating VOCs may be one of the mechanisms responsible for this activity. Similarly, Elek *et al.* (2009) observed 10 of 12 tested *T. boeoticum* and *T. monococcum* accessions had reduced number of settled *R. padi* alate, compared to modern wheat. The tested diploid accessions also reduced aphid fecundity, indicating non-VOC-mediated resistance mechanisms are also present. *T. monococcum* MDR045 and MDR049, previously identified as aphid-resistant by Elek *et al.* (2009), showed reduced numbers of *R. padi* and *S. avenae* and increased presence of aphid predators in field trials.51 VOC extracts from *R. padi*-infested and uninfested MDR049 induced antixenotic activity against *R. padi,* with heptanal, octanal, decanal, 4-ethylbenzaldehyde, 2,4-dimethyl-1-pentene and 4,4-dimethyl-2-pentene reported as potentially responsible for antixenosis.36 Similarly, VOC extracts from *S. avenae*-infested MDR049 and MDR045 induced antixenosis against *S. avenae,* with 21 compounds identified and confirmed as being responsible for this activity.35 The same components were identified in aphid-susceptible *T. monococcum* MDR037 and *T. aestivum* Solstice, indicating compound ratios in VOC blends play an important role in antixenosis,35 in line with insect host location theory.25

*Microbiomes and VOC-mediated aphid resistance in wheat*

Tri-trophic crop-aphid-microbe/virus interactions have also been shown to alter VOC-mediated aphid resistance in wheat (Figure 2). VOCs from *Fusarium graminearum* ((Schwein.) Petch)-infected wheat induce an antixenotic response against *S. avenae* in olfactometry assays, with 2-pentadecanone and 2-heptanone as key compounds responsible for this activity.52 Conversely, BYDV infection of wheat increased *R. padi* preference compared to un-infected wheat,32 with nonanal, (*Z*)-3-hexenyl acetate, decanal, an unknown isomer of caryophyllene and undecane identified as the active compounds.32 The same study observed that BYDV-induced preference is lost in viruliferous aphids, which ecologically would facilitate the spread of BYDV to other non-infected hosts. It should be noted that a similar response has also been documented in wheat-*S. graminum*-BYDV interactions.53 In contrast, heptanal, octanal, nonanal and decanal were found in higher concentrations in headspace extracts from *T. aestivum* inoculated with endophytic entomopathogenic fungi *Beauveria bassiana* ((Bals.-Criv.) Vuill.) and *Metarhizium acridum* ((Driver & Milner) J.F. Bisch., Rehner & Humber), eliciting increased preference in both BYDV viruliferous and non-viruliferous *R. padi*.54 A similar preference response was observed in *Myzus persicae* for *Capsicum anuum* (L.) inoculated with either *B. bassiana* or *Akanthomyces muscarius* ((Petch) Spatafora, Kepler & B. Shrestha).55

**Figure 2:** External factors influencing natural product-based aphid resistance mechanisms in wheat. 1: Herbivore-induced plant volatiles (HIPVs), 2: Abiotic stresses (e.g. heat and drought), 3: Aboveground microbial interactions including beneficial and pathogenic microbes, 4: Aphid feeding and 5: Microbial rhizosphere interactions. Created in BioRender. Birkett, M. (2024) BioRender.com/I12m481.



*Plant-plant communication and VOC resistance to aphids*

In addition to repelling incoming aphids from the plant and attracting natural enemies, aphid-induced HIPVs play a role in plant-plant communication by ‘priming’ neighbouring undamaged plants for enhanced aphid resistance (Figure 2). The priming effect of aphid-induced HIPVs on wheat and other cereals was extensively investigated by Pettersson, Quiroz and Fahad (1996), showing that defence priming is species-specific for both aphid and plant host. Variation in priming responses were observed for *S. avenae, R. padi* and *M. dirhodum* in barley, oat and wheat hosts. For example, *S. avenae*-induced wheat HIPVs primed un-infested wheat to produce VOCs inducing an antixenotic response against *S. avenae* but not *R. padi.*45 6-Methyl-5-hepten-2-one, in addition to 2-tridecanone and (*E*)-2-hexen-1-ol, were shown to prime *T. aestivum* Beijing837 to induce lipoxygenase activity and reduce *S. avenae* feeding and population growth.56 These studies indicate that 6-methyl-5-hepten-2-one and 6-methyl-5-hepten-2-ol play a role in indirect aphid resistance of Beijing837 by priming the plant`s jasmonic acid-mediated defence response and attracting aphid predators. Nonanal, octanal and benzaldehyde are all produced in higher concentrations in mixed *T. aestivum* Florence-Aurora and Forment cultures, which was attributed to its reduced attractiveness to *S. avenae* when compared to Florence-Aurora monoculture.37 The plant phytohormone *cis*-jasmone, released as a HIPV, induces wheat VOCs which stimulate preference in the aphid predators *Coccinella septempunctata* (L.) and *A. ervi.*57,58

1. **Development-modifying resistance mechanisms (antibiosis)**

Development-modifying aphid resistance mechanisms are either metabolite-based or morphological in nature (such as phloem occlusion). Unlike chewing pests, the specialised feeding mechanism of aphids means they mostly bypass chemical defences in leaf tissues apart from those in the xylem and phloem 12. Secondary metabolites are widely known to play a role in plant defence against pests, including aphids. However, primary metabolites also contribute to aphid resistance in wheat.

*Primary metabolites*

The primary nutritional source for the aphid is host phloem. Although it may not be a direct defence response, reduced phloem sap quality can negatively influence aphid survival, enhancing any direct effects of secondary metabolites. Furthermore, primary metabolites act as feeding stimulants during aphid assessment of host suitability, so reduced levels lower chances of host acceptance.59 Primary metabolite, particularly carbohydrate and amino acid, content in the phloem sap of *T. monococcum* MDR049 is lower than that of the aphid-susceptible *T. aestivum* Solstice and *T. monococcum* MDR037, which is partly attributed to the reduced development and fecundity of *R. padi* on MDR049.60 Interestingly, MDR049 showed increased levels of asparagine and glycine upon aphid feeding in addition to threonine and glutamine.60 Whether the increase of these amino acids has a direct effect on aphid survival is still unknown; however, they do not outweigh the effects of the reduced carbohydrate and remaining amino acid content observed in MDR049 phloem sap.60 Similarly, higher primary metabolite gene expression was observed in the tetraploid *T. turgidum* Zavitan which, in addition to other mechanisms, may contribute to the lack of aphid resistance observed in this accession compared to *T. turgidum* Svevo and *T. aestivum* Chinese Spring.61 Effects of abiotic stresses on primary metabolism have gained increased attention because of their effect on aphid survival. Field trials with *T. aestivum* Zhou 22 grown under mild drought conditions showed increased total amino acid concentration, specifically that of arginine, isoleucine, leucine, lysine, glycine and cysteine, which was attributed to increased *S. avenae* abundance and population growth rate.62 Conversely, continuous and pulsed drought stress reduced *S. avenae* growth rate and survival in *T. aestivum* Tybalt, which was partly attributed to reduced levels of sucrose and citric acid, increased levels of proline and asparagine and a relative overall lower concentration of most amino acids in phloem sap.63 These studies demonstrate that lower general primary metabolite concentrations are linked to reduced aphid survival. Abiotic stress-induced changes in primary metabolites have been shown to influence aphid resistance; however, contrasting results indicate that such changes are accession-specific (Figure 2). This highlights the need to assess how abiotic stresses influence primary metabolism and subsequent aphid performance. The effects of abiotic stresses may in turn increase the aphid resistance of currently susceptible wheat varieties via reduced phloem sap quality, but this may come at a cost to lower grain quality.

*Secondary metabolites*

Leaf secondary metabolites have been extensively studied in their role in plant defence against aphids.12 Many are often detrimental to plant health in their active form and are thus either stored or transported in an inactive state and become activated upon contact with enzymes stored in separate cellular compartments. Activation is facilitated by chewing herbivores, where physical rupturing of leaf cells brings the inactive metabolite and enzyme in contact, creating the active form. Due to their specialised feeding behaviour, aphids mostly bypass secondary metabolite-associated defence responses, and leaf secondary metabolites involved in aphid defence are only induced upon detection of aphid feeding.12 Physicochemical properties of secondary metabolites also play a key role in activity: non-polar compounds are more toxic as they passively cross cellular membranes of the aphid, whilst polar compounds are excreted in honeydew, imparting minimal damage.64 Aphids also actively detoxify secondary metabolites.12,65,66 The most common leaf secondary metabolites associated with aphid defence responses include alkaloids, cardiac glycosides, benzoxazinoids (BXs) and glucosinolates, all of which have been reviewed.12,67

Benzoxazinoids (BXs), also known as hydroxamic acids, are the most commonly associated leaf secondary metabolites involved in cereal defence against aphids. BXs are predominantly found in maize and wheat, the most common of which are shown in Table 1. They contribute to i) resistance against chewing herbivores,68 fungal pathogens,69 and aphids,43,70 ii) allelochemical activity,71,72 iii) abiotic stress tolerance, 73,74 and iv) iron chelation.75 Predominantly stored in their inactive glucoside form, BXs are activated by glucosidases upon herbivore damage or after ingestion by the pest.67 2,4-Dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA) and its glucoside 2,4-dihydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-one 2-O-glucoside (DIMBOA-Glc) are the most common BXs in maize; however, the less common 2-hydroxy-4,7-dimethoxy-1,4-benzoxazin-3-one glucoside (HDMBOA-Glc) has higher aphid toxicity due to increased instability, spontaneously breaking down into its toxic form in the absence of glucosidases.76 The reduced stability of HDMBOA-Glc results in autotoxicity to the plant and is therefore often only produced upon detection of aphid feeding.76 The biosynthetic pathway and regulation of BXs have been characterized in maize and partially in wheat,77,78 and similarities are observed in herbivore-induced BX regulation between species.79 Wheat BX content is highly variable, high concentrations correlating with higher, albeit partial, aphid resistance.38,40,41,44,60 Susceptibility to BXs is aphid species-specific in *T. turgidum* Svevo, where aphid-induced DIMBOA and HDMBOA-Glc elicit resistance to *S. avenae* andpartial resistance to *R. padi*, with no resistance to *S. graminum.*40 In addition to reducing aphid performance, BXs also show aphid antibiotic properties;44 for example, high BX content in the wheat-relative *Aegilops* *sp.* is attributed to reduced *R. padi* fecundity.39 The presence of BXs in *Ae*. *speltoides* (Tasuch.) indicates BX biosynthesis in tetraploid and hexaploid wheat is derived from the B genome. Wheat BX content is influenced by external chemical stimuli, with exposure to *cis*-jasmone reducing *S. avenae* settling and reproduction and increasing BX levels.80,81 Apart from their direct effect on aphid performance, BXs act as signalling molecules, which may contribute to aphid resistance, further emphasizing the blurred line between primary and secondary metabolite functions. For example, DIMBOA plays a signalling role in the induction of callose deposition upon aphid feeding.79 Furthermore, BXs are involved in the regulation of phenolic compounds linked to aphid resistance, with the overexpression of maize BX *O-methyltransferases* in wheat accompanied by an increase in phenylpropanoid ferulic acid concentrations.79 BXs play a role in shaping both above- and belowground microbiomes,82 which have been shown to affect aphid resistance (Figure 2).83,84 BXs are not the only leaf secondary metabolites involved in wheat-derived aphid resistance, as diploid *T. monococcum*, *T. boeticum* and *Ae. longissima* (Schewing. & Muschl.) are resistant against *R. padi* but have non-detectable levels of BXs.39,50 Specifically, the potential involvement of phloem occlusion as an aphid resistance mechanism, in addition to the reduced levels of primary metabolites discussed above, confer resistance in *T. monococcum* MDR049.60 However, other leaf secondary metabolites may also play a role in aphid defence of MDR049.

Cereal flavonoids are common antifeedant compounds against chewing herbivores and negatively impact the cereal aphids *S. graminum* and *R. maidis* (Fitch).85–87 There is some evidence which suggests that flavonoid and phenolic content of wheat play a role in *S. avenae* and *R. padi* resistance. Reduced aphid infestation on six bread wheat varieties in the field was accompanied by increased total phenol content.88 Similarly, total phenol and tannin content of *T. aestivum* W0923 was attributed to resistance against *R. padi.*89 S*. avenae*-resistant *T. aestivum* Yongliang No.15 and Ganchun No.18 showed an aphid-induced increase in total flavonoid content, which was correlated to their antibiotic activity.90 The same study showed *S. avenae* feeding on susceptible *T. aestivum* accessions decreased both total phenol and flavonoid content, indicating suppression of plant defence responses. Similarly, *S. avenae* induced an increase in apigenin, luteolin, (+)-catechin and (-)-epichatechin content in aphid-resistant *Triticale* Lamberto, suggesting the increased production of these flavonoids is linked to the accession`s aphid resistance.91 Neither of these studies directly investigated the effects of flavonoids on aphid survival, and therefore the link between flavonoid/phenol content and aphid resistance, although promising, is correlative and requires confirmation. Similar to primary metabolites, abiotic stresses have been shown to influence both flavonoid and BX production in wheat,67,92 which in turn could influence SM-based aphid antibiotic resistance. How abiotic stresses positively or negatively influence SM-based aphid antibiotic resistance requires further investigation and may be genotype-dependent.

1. **Conclusions**

The need to transition away from insecticide use in managing cereal aphid populations has spurred an increased interest in screening studies to identify aphid resistance across diploid, tetraploid and hexaploid wheat.48,50,93–99 Despite promising results, further investigation is still required to fully elucidate the resistance mechanisms, a crucial step for the eventual incorporation of these traits into modern elite wheat via either traditional breeding or genetic engineering approaches.

VOC-mediated antixenosis holds promise as an effective resistance mechanism against *S. avenae* and *R. padi*. However, as VOC blend composition plays a crucial role in the type of activity elicited, i.e. either attraction or repellence, the complex interaction between blend components and their regulation pose a major challenge for the incorporation of VOC-mediated aphid resistance into modern wheat. For example, a gene encoding for the aphid alarm pheromone (*E*)-b-farnesene was introduced into the aphid-susceptible wheat line *T. aestivum* Cadenza, which was successful in eliciting antixenotic resistance against *S. avenae*, *R. padi* and *M. dirhodum* and attraction of the aphid parasitoid *A. ervi* under laboratory conditions; however, these activities were not translated into the field.100 Despite these challenges, wheat lines possessing aphid antixenosis may be incorporated into IPM strategies as intercrops within a push-pull system. Pathogen-plant and plant-plant interactions alter VOC blend activity and the subsequent resistance mechanisms they induce (Figure 2). Future studies should take these interactions into account when investigating VOC-mediated aphid resistance mechanisms before their integration into modern wheat and use in the field.

Expression of BX secondary metabolites in wheat is insufficient to impart complete aphid resistance, however the BX biosynthetic pathway has been extensively elucidated in maize, with orthologs and paralogs of these genes identified in wheat.101,102 Investigations into the transcriptional regulation of the BX biosynthetic pathway have been reported in maize and wheat,74,103 which will be crucial in the exploitation of this pathway to impart its associated resistance traits. Further investigations are required to identify other secondary metabolite classes, and their biosynthetic pathways, involved in *S. avenae* and *R. padi* resistance. The signalling roles of BXs, particularly in the recruitment of rhizosphere microbes (Figure 2), should be investigated further within the wheat-aphid system to determine whether particular microbial communities enhance aphid resistance traits. Additionally, the effect of climate-related abiotic factors on aphid resistance needs further exploration to determine the durability of such traits (Figure 2). Similar to BXs, flavonoids shape belowground plant-microbe interactions,104 which in turn may affect wheat aphid resistance, an area of research that deserves investigation. This is further compounded by the possible involvement of phenolic compounds in BYDV resistance conferred by *’bdv2’*, a gene which has been successfully bred into modern elite wheat.20,23

Overall, natural product-based resistance mechanisms are major contributing factors to aphid resistance in wheat. Further research is required to fully elucidate the metabolites involved, their biosynthetic pathways and the influence abiotic factors have on these interactions. Furthermore, the availability of national germplasms provides an underutilized resource for the identification of further aphid resistant wheat accessions and traits. Ongoing research in this field is promising and, in addition to a further understanding of the molecular mechanisms involved in the induction of aphid resistance and suppression of defence responses by aphids, it holds potential for the development of resistant wheat lines against *S. avenae* and *R. padi* to alleviate reliance on the use of insecticides and enhance food security.

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**Competing Interests**

The authors declare there are no competing interests.

**Author Contributions**

ANB, JV, JCC and MAB were involved in conceptualisation of the manuscript. ANB contributed to writing. JV, JCC and MAB revised and supervised manuscript.

**References**

1. Aradottir, G. I. & Crespo-Herrera, L. Host plant resistance in wheat to barley yellow dwarf viruses and their aphid vectors: a review. *Curr. Opin. Insect Sci.* **45**, 59–68 (2021).

2. Gildow, F. E. & Rochow, W. F. Barley Yellow Dwarf in California: Vector Competence and Luteovirus Identification. *Plant Dis.* **67**, 140–143 (1982).

3. Will, T. & Vilcinskas, A. The structural sheath protein of aphids is required for phloem feeding. *Insect Biochem. Mol. Biol.* **57**, 34–40 (2015).

4. Rabbinge, R., Drees, E. M., van der Graaf, M., Verberne, F. C. M. & Wesselo, A. Damage effects of cereal aphids in wheat. *Netherlands J. Plant Pathol.* **87**, 217–232 (1981).

5. Mc Namara, L. *et al.* Management of yellow dwarf disease in Europe in a post‐neonicotinoid.pdf. *Pest Manag. Sci.* **76**, 2276–2285 (2020).

6. Walsh, L. E., Schmidt, O., Williamson, M. S. & Gaffney, M. T. In-field prevalence of resistant grain aphid *Sitobion avenae* (Fabricius). *Biol. Environ.* **120B**, 29–38 (2020).

7. Chen, Y., Li, R., Li, B. & Meng, L. Biochar applications decrease reproductive potential of the English grain aphid *Sitobion avenae* and upregulate defense-related gene expression. *Pest Manag. Sci.* **75**, 1310–1316 (2019).

8. Luo, K., Zhao, H., Wang, X. & Kang, Z. Prevalent Pest Management Strategies for Grain Aphids: Opportunities and Challenges. *Front. Plant Sci.* **12**, 1–12 (2022).

9. Åhman, I., Kim, S. Y. & Zhu, L. H. Plant Genes Benefitting Aphids—Potential for Exploitation in Resistance Breeding. *Front. Plant Sci.* **10**, (2019).

10. Sun, Y. *et al.* Silencing an essential gene involved in infestation and digestion in grain aphid through plant-mediated RNA interference generates aphid-resistant wheat plants. *Plant Biotechnol. J.* **17**, 852–854 (2019).

11. Tolmay, V. L., Sydenham, S. L., Sikhakhane, T. N., Nhlapho, B. N. & Tsilo, T. J. Elusive diagnostic markers for Russian wheat aphid resistance in bread wheat: Deliberating and reviewing the status quo. *Int. J. Mol. Sci.* **21**, 1–22 (2020).

12. Züst, T. & Agrawal, A. A. Mechanisms and evolution of plant resistance to aphids. *Nat. Plants* **2**, 1–9 (2016).

13. Erb, M. & Kliebenstein, D. J. Plant Secondary Metabolites as Defenses, Regulators, and Primary Metabolites: The Blurred Functional Trichotomy. *Plant Physiol.* **184**, 39–52 (2020).

14. Choudhury, S. *et al.* Barley yellow dwarf viruses: infection mechanisms and breeding strategies. *Euphytica* **213**, 1–22 (2017).

15. Valenzuela, I. & Hoffmann, A. A. Effects of aphid feeding and associated virus injury on grain crops in Australia. *Austral Entomol.* **54**, 292–305 (2015).

16. Gong, P. *et al.* Field evolved resistance to pyrethroids, neonicotinoids, organophosphates and macrolides in *Rhopalosiphum padi* (Linnaeus) and *Sitobion avenae* (Fabricius) from China. *Chemosphere* **269**, 128747 (2021).

17. Foster, S. & Leybourne, D. J. *Final Report Pyrethroid Sensitivity in UK Cereal Aphids*. https://ahdb.org.uk/pyrethroid-sensitivity-in-uk-cereal-aphids-2019-20 (2021).

18. Fontaine, S., Caddoux, L. & Barrès, B. First report of the kdr pyrethroid resistance mutation in a French population of the English grain aphid, Sitobion avenae. *Crop Prot.* **165**, (2023).

19. Leybourne, D. J., Melloh, P. & Martin, E. A. Common facultative endosymbionts do not influence sensitivity of cereal aphids to pyrethroids. *Agric. For. Entomol.* **25**, 344–354 (2023).

20. Brown, J. K. M. *Achievements in Breeding Cereals with Durable Disease Resistance in Northwest Europe*. *Achieving durable disease resistance in cereals* (Burleigh dodds Sceince, 2022). doi:10.1201/9781003180715-31.

21. Zhang, Z., Lin, Z. & Xin, Z. Research progress in BYDV resistance genes derived from wheat and its wild relatives. *J. Genet. Genomics* **36**, 567–573 (2009).

22. Anderson, J. A. *et al.* Registration of ‘MN‐Washburn’ hard red spring wheat containing Barley yellow dwarf virus resistance gene bdv2. *J. Plant Regist.* **15**, 490–503 (2021).

23. Choudhury, S. *et al.* Agronomical, biochemical and histological response of resistant and susceptible wheat and barley under BYDV stress. *PeerJ* **2018**, 1–21 (2018).

24. Wang, X. *et al.* Wheat resistome in response to barley yellow dwarf virus infection. *Funct. Integr. Genomics* **13**, 155–165 (2013).

25. Bruce, T. J. A., Wadhams, L. J. & Woodcock, C. M. Insect host location: A volatile situation. *Trends Plant Sci.* **10**, 269–274 (2005).

26. Bruce, T. J. A. & Pickett, J. A. Perception of plant volatile blends by herbivorous insects - Finding the right mix. *Phytochemistry* **72**, 1605–1611 (2011).

27. Quiroz, A. & Niemeyer, H. M. Olfactometer-assessed responses of aphid *Rhopalosiphum padi* to wheat and oat volatiles. *J. Chem. Ecol.* **24**, 113–124 (1998).

28. Guo, G. & Liu, Y. Behavioral responses of *Macrosiphum avenae* and *Rhopalosiphum padi* to wheat plant volatiles induced by aphids feeding. *Chin. Bull. Entomol.* **42**, 534–536 (2005).

29. Hai-Cui, X. *et al.* Effect of wheat plant volatiles on aphids and associated predator behavior: selection of efficient infochemicals for field study. *Chinese J. Appl. Entomol.* **51**, 1470–1478 (2014).

30. Schröder, M. L., Glinwood, R., Webster, B., Ignell, R. & Krüger, K. Olfactory responses of *Rhopalosiphum padi* to three maize, potato, and wheat cultivars and the selection of prospective crop border plants. *Entomol. Exp. Appl.* **157**, 241–253 (2015).

31. Webster, B., Gezan, S., Bruce, T., Hardie, J. & Pickett, J. Between plant and diurnal variation in quantities and ratios of volatile compounds emitted by Vicia faba plants. *Phytochemistry* **71**, 81–89 (2010).

32. Medina-Ortega, K. J., Bosque-Perez, N. A., Ngumbi, E., Jiménez-Martínez, E. S. & Eigenbrode, S. D. *Rhopalosiphum padi* (Hemiptera: Aphididae) responses to volatile cues from barley yellow dwarf virus-infected wheat. *Environ. Entomol.* **38**, 836–845 (2009).

33. Quiroz, A., Pettersson, J., Pickett, J. A., Wadhams, L. & Niemeyer, H. M. Key compounds in a spacing pheromone in the bird cherry-oat aphid, *Rhopalosiphum padi* (L.)(Hemiptera, Aphididae). *J. Chem. Ecol.* **23**, 2599–2607 (1997).

34. Zhang, Y., Fan, J., Francis, F. & Chen, J. Watery Saliva Secreted by the Grain Aphid *Sitobion avenae* Stimulates Aphid Resistance in Wheat. *J. Agric. Food Chem.* **65**, 8798–8805 (2017).

35. Borg, A. N. *et al.* Characterisation of aphid antixenosis in aphid‐resistant ancestor wheat, *Triticum monococcum*. *Pest Manag. Sci.* (2024) doi:10.1002/ps.8380.

36. Simon, A. L. Unravelling cereal aphid interactions with ancestral wheat *Triticum monococcum* [Thesis].[Nottingham, UK]: University of Nottingham; 2020.

37. Tous-fandos, A., Gallinger, J., Enting, A., Chamorro-Lorenzo, L., Sans Serra, F.X., Ninkovic, V. Alterations in the odor profile of plants in cultivar mixtures affect aphid host-location behavior. *Front. Plant. Sci.* **14**:1186425(2023).

38. Elek, H. *et al.* The potential of hydroxamic acids in tetraploid and hexaploid wheat varieties as resistance factors against the bird-cherry oat aphid, *Rhopalosiphum padi*. *Ann. Appl. Biol.* **162**, 100–109 (2012).

39. Elek, H. *et al.* Hydroxamic acids in Aegilops species and effects on *Rhopalosiphum padi* behaviour and fecundity. *Bull. Insectology* **66**, 213–220 (2013).

40. Shavit, R., Batyrshina, Z. S., Dotan, N. & Tzin, V. Cereal aphids differently affect benzoxazinoid levels in durum wheat. *PLoS One* **13**, 1–14 (2018).

41. Givovich, A. & Niemeyer, H. M. Comparison of the effect of hydroxamic acids from wheat on five species of cereal aphids. *Entomol. Exp. Appl.* **74**, 115–119 (1995).

42. Bohidar, K., Wratten, S. D. & Niemeyer, H. M. Effects of hydroxamic acids on the resistance of wheat to the aphid *Sitobion avenae*. *Ann. Appl. Biol.* **109**, 193–198 (1986).

43. Givovich, A. & Niemeyer, H. M. Hydroxamic acids affecting barley yellow dwarf virus transmission by the aphid *Rhopalosiphum padi*. *Entomol. Exp. Appl.* **59**, 79–85 (1991).

44. Givovich, A., Sandström, J., Niemeyer, H. M. & Pettersson, J. Presence of a hydroxamic acid glucoside in wheat phloem sap, and its consequences for performance of *Rhopalosiphum padi* (L.) (Homoptera: Aphididae). *J. Chem. Ecol.* **20**, 1923–1930 (1994).

45. Pettersson, J., Quiroz, A. & Fahad, A. E. Aphid antixenosis mediated by volatiles in cereals. *Acta Agric. Scand. Sect. B Soil Plant Sci.* **46**, 135–140 (1996).

46. Ninkovic, V., Ahmed, E., Glinwood, R. & Pettersson, J. Effects of two types of semiochemical on population development of the bird cherry oat aphid *Rhopalosiphum padi* in a barley crop. *Agric. For. Entomol.* **5**, 27–34 (2003).

47. Liu, Y., Wang, W. L., Guo, G. X. & Ji, X. L. Volatile emission in wheat and parasitism by Aphidius avenae after exogenous application of salivary enzymes of *Sitobion avenae*. *Entomol. Exp. Appl.* **130**, 215–221 (2009).

48. Correa, L. D. J. *et al.* A Comprehensive Analysis of Wheat Resistance to *Rhopalosiphum padi* (Hemiptera: Aphididae) in Brazilian Wheat Cultivars. *J. Econ. Entomol.* **113**, 1493–1503 (2020).

49. Liu, X. *et al.* Identification of Differentially Expressed Genes in Resistant Tetraploid Wheat (*Triticum turgidum*) under *Sitobion avenae* (F.) Infestation. *Int. J. Mol. Sci.* **23**, (2022).

50. Elek, H. *et al.* Aphid resistance in wheat varieties. *Commun. Agric. Appl. Biol. Sci.* **74**, 233–241 (2009).

51. Simon, A. L., Caulfield, J. C., Hammond-Kosack, K. E., Field, L. M. & Aradottir, G. I. Identifying aphid resistance in the ancestral wheat *Triticum monococcum* under field conditions. *Sci. Rep.* **11**, 1–12 (2021).

52. Drakulic, J. *et al.* Sharing a host plant (Wheat [*Triticum aestivum*]) Increases the fitness of F*usarium graminearum* and the severity of fusarium head blight but reduces the fitness of grain aphids (*Sitobion avenae*). *Appl. Environ. Microbiol.* **81**, 3492–3501 (2015).

53. Hu, Z. *et al.* Barley yellow dwarf virus-infected wheat plant modulated selection behavior of vector aphids. *J. Pest Sci. (2004).* **95**, 1273–1285 (2022).

54. Fingu-Mabola, J. C., Martin, C., Bawin, T., Verheggen, F. J. & Francis, F. Does the infectious status of aphids influence their preference towards healthy, virus-infected and endophytically colonized plants? *Insects* **11**, 1–16 (2020).

55. Wilberts, L. *et al.* Impact of endophytic colonization by entomopathogenic fungi on the behavior and life history of the tobacco peach aphid *Myzus persicae* var. nicotianae. *PLoS One* **17**, 1–17 (2022).

56. Zhao, L. Y. *et al.* Biochemical and molecular characterizations of *Sitobion avenae* -induced wheat defense responses. *Crop Prot.* **28**, 435–442 (2009).

57. Birkett, M. A. *et al.* New roles for cis-jasmone as an insect semiochemical and in plant defense. *Proc. Natl. Acad. Sci. U. S. A.* **97**, 9329–9334 (2000).

58. Bayram, A. & Tonğa, A. cis-Jasmone treatments affect pests and beneficial insects of wheat (*Triticum aestivum* L.): the influence of doses and plant growth stages. *Crop Prot.* **105**, 70–79 (2018).

59. Schoonhoven, L. M., van Loon, J. J. A. & Dicke, M. *Insect-Plant Biology*. (Oxford University Press, Oxford, 2006).

60. Greenslade, A. F. C. *et al.* *Triticum monococcum* lines with distinct metabolic phenotypes and phloem-based partial resistance to the bird cherry-oat aphid *Rhopalosiphum padi*. *Ann. Appl. Biol.* **168**, 435–449 (2016).

61. Batyrshina, Z. S., Yaakov, B., Shavit, R., Singh, A. & Tzin, V. Comparative transcriptomic and metabolic analysis of wild and domesticated wheat genotypes reveals differences in chemical and physical defense responses against aphids. *BMC Plant Biol.* **20**, 1–20 (2020).

62. Cui, H., Wang, L., Reddy, G. V. P. & Zhao, Z. Mild Drought Facilitates the Increase in Wheat Aphid Abundance by Changing Host Metabolism. *Ann. Entomol. Soc. Am.* **114**, 79–83 (2021).

63. Stallmann, J., Pons, C. A. A., Schweiger, R. & Müller, C. Time point- and plant part-specific changes in phloem exudate metabolites of leaves and ears of wheat in response to drought and effects on aphids. *PLoS One* **17**, 1–18 (2022).

64. Züst, T. & Agrawal, A. A. Population growth and sequestration of plant toxins along a gradient of specialization in four aphid species on the common milkweed *Asclepias syriaca.* *Funct. Ecol.* **30**, 547–556 (2016).

65. Roberts, M. F. & Wink, M. *Alkaloids: Biochemistry, Ecology and Medicinal Applications*. (Springer Science, 1998).

66. Singh, K. S. *et al.* The genetic architecture of a host shift: An adaptive walk protected an aphid and its endosymbiont from plant chemical defenses. *Sci. Adv.* **6**, (2020).

67. Robert, C. A. M. & Mateo, P. The Chemical Ecology of Benzoxazinoids. *Chimia (Aarau).* **76**, 928–938 (2022).

68. Glauser, G. *et al.* Induction and detoxification of maize 1,4-benzoxazin-3-ones by insect herbivores. *Plant J.* **68**, 901–911 (2011).

69. Duan, S. *et al.* Integrated transcriptome and metabolite profiling highlights the role of benzoxazinoids in wheat resistance against Fusarium crown rot. *Crop J.* **10**, 407–417 (2022).

70. Hansen, L. M. Effect of 6-Methoxybenzoxazolin-2-one ( MBOA ) on the Reproduction Rate of the Grain Aphid ( *Sitobion avenae* F .). *J. Agric. Food Chem.* **54**, 1031–1035 (2006).

71. Yedra, V. Á. *et al.* Testing the role of allelochemicals in different wheat cultivars to sustainably manage weeds. *Pest Manag. Sci.* **79**, 2625–2638 (2023).

72. Belz, R. G. & Hurle, K. Differential Exudation of Two Benzoxazinoids - One of the Determining Factors for Seedling Allelopathy of Triticeae Species. *J. Agric. Food Chem.* **53**, 250–261 (2005).

73. Bi, H. *et al.* Identification and characterization of wheat drought-responsive MYB transcription factors involved in the regulation of cuticle biosynthesis. *J. Exp. Bot.* **67**, 5363–5380 (2016).

74. Batyrshina, Z. S., Shavit, R., Yaakov, B., Bocobza, S. & Tzin, V. The transcription factor TaMYB31 regulates the benzoxazinoid biosynthetic pathway in wheat. *J. Exp. Bot.* **73**, 5634–5649 (2022).

75. Hu, L. *et al.* Plant iron acquisition strategy exploited by an insect herbivore. *Science (80-. ).* **361**, 694–697 (2018).

76. Meihls, L. N. *et al.* Natural variation in maize aphid resistance is associated with 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one glucoside methyltransferase activity. *Plant Cell* **25**, 2341–2355 (2013).

77. Niculaes, C., Abramov, A., Hannemann, L. & Frey, M. Plant protection by benzoxazinoids—recent insights into biosynthesis and function. *Agronomy* **8**, (2018).

78. Stahl, E. New insights into the transcriptional regulation of benzoxazinoid biosynthesis in wheat. *J. Exp. Bot.* **73**, 5358–5360 (2022).

79. Li, B. *et al.* Convergent evolution of a metabolic switch between aphid and caterpillar resistance in cereals. *Sci. Adv.* **4**, 1–15 (2018).

80. Moraes, M. C. B. *et al.* cis -Jasmone induces accumulation of defence compounds in wheat , *Triticum aestivum*. *Phytochemistry* **69**, 9–17 (2008).

81. Bruce, T. J. A., Martin, J. L., Pickett, J. A., Pye, B. J. & Smart, L. E. cis -Jasmone treatment induces resistance in wheat plants against the grain aphid, *Sitobion avenae* (Fabricius)(Homoptera : Aphididae ). *Pest Manag. Sci.* **59**, 1031–1036 (2003).

82. Cadot, S. *et al.* Specific and conserved patterns of microbiota-structuring by maize benzoxazinoids in the field. *Microbiome* **9**, 1–19 (2021).

83. Charters, M. D., Durant, E. K., Sait, S. M. & Field, K. J. Impacts of aphid herbivory on mycorrhizal growth responses across three cultivars of wheat. *Plants People Planet* **4**, 655–666 (2022).

84. Simon, A. L., Wellham, P. A. D., Aradottir, G. I. & Gange, A. C. Unravelling mycorrhiza-induced wheat susceptibility to the English grain aphid *Sitobion avenae*. *Sci. Rep.* **7**, 1–11 (2017).

85. Simmonds, M. S. J. Flavonoid-insect interactions: Recent advances in our knowledge. *Phytochemistry* **64**, 21–30 (2003).

86. Dreyer, D. L. & Jones, K. C. Feeding deterrency of flavonoids and related phenolics towards *Schizaphis graminum* and *Myzus persicae*: Aphid feeding deterrents in wheat. *Phytochemistry* **20**, 2489–2493 (1981).

87. Kariyat, R. R. *et al.* Sorghum 3-Deoxyanthocyanidin Flavonoids Confer Resistance against Corn Leaf Aphid. *J. Chem. Ecol.* 502–514 (2019) doi:10.1007/s10886-019-01062-8.

88. Kaur, H., Salh, P. K. & Singh, B. Role of defense enzymes and phenolics in resistance of wheat crop (*Triticum aestivum* L.) towards aphid complex. *J. Plant Interact.* **12**, 304–311 (2017).

89. Xu, Y., Guo, H., Geng, G., Zhang, Q. & Zhang, S. Changes in defense-related enzymes and phenolics in resistant and susceptible common wheat cultivars under aphid stress. *Acta Physiol. Plant.* **43**, 1–9 (2021).

90. Zhang, K. X. *et al.* Responses of Six Wheat Cultivars (*Triticum aestivum*) to Wheat Aphid (*Sitobion avenae*) Infestation. *Insects* **13**, (2022).

91. Czerniewicz, P., Sytykiewicz, H., Durak, R., Borowiak-Sobkowiak, B. & Chrzanowski, G. Role of phenolic compounds during antioxidative responses of winter triticale to aphid and beetle attack. *Plant Physiol. Biochem.* **118**, 529–540 (2017).

92. Shah, A. & Smith, D. L. Flavonoids in agriculture: Chemistry and roles in, biotic and abiotic stress responses, and microbial associations. *Agronomy* **10**, (2020).

93. Migui, S. M. & Lamb, R. J. Seedling and adult plant resistance to *Sitobion avenae* (Hemiptera: Aphididae) in *Triticum monococcum* (Poaceae), an ancestor of wheat . *Bull. Entomol. Res.* **94**, 35–46 (2004).

94. Migui, S. M. & Lamb, R. J. Patterns of resistance to three cereal aphids among wheats in the genus Triticum (Poaceae) . *Bull. Entomol. Res.* **93**, 323–333 (2003).

95. Radchenko, E. E. Resistance of Triticum species to cereal aphids. *Czech J. Genet. Plant Breed.* **47**, 2009–2012 (2011).

96. Hu, X. S. *et al.* Resistance of wheat accessions to the english grain aphid *Sitobion avenae*. *PLoS One* **11**, 1–17 (2016).

97. Aradottir, G. I., Martin, J. L., Clark, S. J., Pickett, J. A. & Smart, L. E. Searching for wheat resistance to aphids and wheat bulb fly in the historical Watkins and Gediflux wheat collections. *Ann. Appl. Biol.* **170**, 179–188 (2017).

98. Di Pietro, J. P., Caillaud, C. M., Chaubet, B., Pierre, J. S. & Trottet, M. Variation in resistance to the grain aphid, *Sitobion avenae* (Sternorhynca: Aphididae), among diploid wheat genotypes: Multivariate analysis of agronomic data. *Plant Breed.* **117**, 407–412 (1998).

99. Liu, X. L. *et al.* Identification of Sitobion avenae F. resistance and genetic diversity of wheat landraces from Qinling Mountains, China. *Cereal Res. Commun.* **46**, 104–113 (2018).

100. Bruce, T. J. A. *et al.* The first crop plant genetically engineered to release an insect pheromone for defence. *Sci. Rep.* **5**, 1–9 (2015).

101. Wu, D., Jiang, B., Ye, C., Timko, M. P. & Fan, L. Horizontal transfer and evolution of the biosynthetic gene cluster for benzoxazinoids in plants. *Plant Commun.* **3**, 100320 (2022).

102. Shavit, R., Batyrshina, Z. S., Yaakov, B., Florean, M. & Tzin, V. The wheat dioxygenase BX6 is involved in the formation of benzoxazinoids in planta and contributes to plant defense against insect herbivores. *Plant Sci.* **316**, (2022).

103. Zhang, C. *et al.* ZmMPK6 and ethylene signalling negatively regulate the accumulation of anti‐insect. *New Phytol.* **229**, 2273–2287 (2021).

104. Wang, L. *et al.* Multifaceted roles of flavonoids mediating plant-microbe interactions. *Microbiome* **10**, 1–13 (2022).