agronomy

MDPI

Review

Flavonoids in Agriculture: Chemistry and Roles in, Biotic and Abiotic Stress Responses, and Microbial Associations

Ateeq Shah and Donald L. Smith *

Department of Plant Science, Macdonald Campus, McGill University,
Sainte-Anne-de-Bellevue, QC H9X 3V9, Canada; Ateeq.Shah@mail.mcgill.ca
* Correspondence: donald.smith@mcgill.ca

Received: 26 June 2020; Accepted: 11 August 2020; Published: 17 August 2020

Abstract: The current world of climate change, global warming and a constantly changing environment have made life very stressful for living entities, which has driven the evolution of biochemical processes to cope with stressed environmental and ecological conditions. As climate change conditions continue to develop, we anticipate more frequent occurrences of abiotic stresses such as drought, high temperature and salinity. Living plants, which are sessile beings, are more exposed to environmental extremes. However, plants are equipped with biosynthetic machinery operating to supply thousands of bio-compounds required for maintaining internal homeostasis. In addition to chemical coordination within a plant, these compounds have the potential to assist plants in tolerating, resisting and escaping biotic and abiotic stresses generated by the external environment. Among certain biosynthates, flavonoids are an important example of these stress mitigators. Flavonoids are secondary metabolites and biostimulants; they play a key role in plant growth by inducing resistance against certain biotic and abiotic stresses. In addition, the function of flavonoids as signal compounds to communicate with rhizosphere microbes is indispensable. In this review, the significance of flavonoids as biostimulants, stress mitigators, mediators of allelopathy and signaling compounds is discussed. The chemical nature and biosynthetic pathway of flavonoid production are also highlighted.

Keywords: flavonoids; biotic and abiotic stress; symbiosis; signaling; rhizobium; AMF; salinity; allelopathy

1. Introduction

Climate change is the most serious threat to current human culture. Escalating global food demand and ever-increasing global warming put humanity in jeopardy. According to ongoing global temperature analysis carried out by NASA's Goddard Institute for Space Studies (GISS) scientists, the average global temperature has increased by about 1 °C since 1880 [1], and it is estimated that every 2 °C rise in global temperature will cause on hundred million human deaths and bring millions of species to the brink of extinction [2]. After fossil fuel burning for energy generation, agriculture is the second-largest contributor to climate change through the emission of greenhouse gases (GHGs) including carbon dioxide (CO_2), methane (CH_4) and nitrous oxide (N_2O) [3]. Commercial fertilizers are very convenient, easy to handle and a rapid source of soil nutrient recharge, however, the toxic and residual effects of synthetic chemicals have altered thinking around this. It is estimated that reductions in mineral fertilizer use could lead to a 20% reduction in GHG emissions [4]. As the world warms, there is an immediate need to adjust what have become inadequate and inappropriate policies. There is an urgency to develop ecofriendly land practices and more sustainable agriculture. The implementation of biobased products, for example, ushering in the use of organic farming,

biofertilizers and biocontrol techniques, will be a progressive step towards sustainable global food security. In this review, we focused on a specific type of biostimulant, flavonoids, and their role in sustainable agriculture. Flavonoids are examples of a versatile set of low molecular weight secondary metabolites with a polyphenolic structure, involved in plant physiological functions, often demonstrating protective effects against biotic and abiotic stresses including UV-B radiation [5], salt stress [6] and drought [7], at least in part by detoxifying the Reactive Oxygen Species (ROS) produced under stress conditions in plants [8,9]. Flavonoids also play a crucial role in plant–microbe associations, predominantly plant–rhizobia and arbuscular mycorrhizal symbioses [10]. Certain flavonoids act as signaling compounds triggering nodule induction by inducing transcription of *nod* genes in rhizobia, the first step in legume–rhizobia symbiotic relationships [11]. In addition, some flavonoids act to combat certain pests and pathogens [12]. Some classes of flavonoids act as color pigments, producing specific hues in leaves and flower petals, helping plants attract pollinators [13]. Moreover, flavonoids have indirect effects on nutrient supply and availability by enhancing mycorrhizal symbioses and colonization of the rhizosphere by beneficial microorganisms [14].

2. Biosynthesis and Classification of Flavonoids

The biosynthesis of distinct flavonoid-based compounds is the result of condensation of one molecule of 4-coumaroyl-CoA (6-carbon) and three molecules of malonyl-CoA, carried out by the enzyme chalcone synthase (CHS). The two major precursors originate from two different pathways of cellular metabolism: the acetate pathway and shikimate pathway providing ring A and ring B, respectively, with chain linkages forming ring C. Ring A is generated from malonyl-CoA synthesized by carboxylation of acetyl-CoA via the acetate pathway, however, ring B along with the linking chain (ring C) is synthesized from coumaroyl-CoA via the shikimate pathway (Figure 1). Coumaroyl-CoA is generated directly from the amino acid phenylalanine by three enzymatic reactions of the phenylpropanoid pathway [15].

The condensation of these aromatic rings by these pathways results in the synthesis of chalcone which will then form flavanone after isomerase-catalyzed cyclization. The later compounds undergo further modifications such as hydroxylation, glycosylation or methylation resulting in the enormous range of flavonoid colors we see today.

Flavonoids are the largest family of natural products; more than nine thousands of these phenolic substances have been found in various plants [16]. Flavonoids have a basic structure containing three phenolic rings, namely A (6 carbon) and B (6-carbon) linked with the central C (3-carbon) ring; C_6-C_3-C_6 which can produce several derivatives and sub-class compounds with distinct substitutions in the basic structure [17]. The major subgroups of flavonoids are; flavonols, flavones, flavanones, flavanonols, flavanols, anthocyanins, isoflavonoids and chalcones [18]. However, based on the attachment of the B ring to the C ring, flavonoids have been classified into three major subgroups: Flavonoids (2-phenylbenzopyrans): The B ring is attached on 2-position of ring C), Isoflavonoids (3-benzopyrans): The B ring is attached on 3-position of ring C) and Neoflavonoids (4-benzopyrans: unlike isoflavonoids; the B ring is attached at 4-position of C ring) [19].

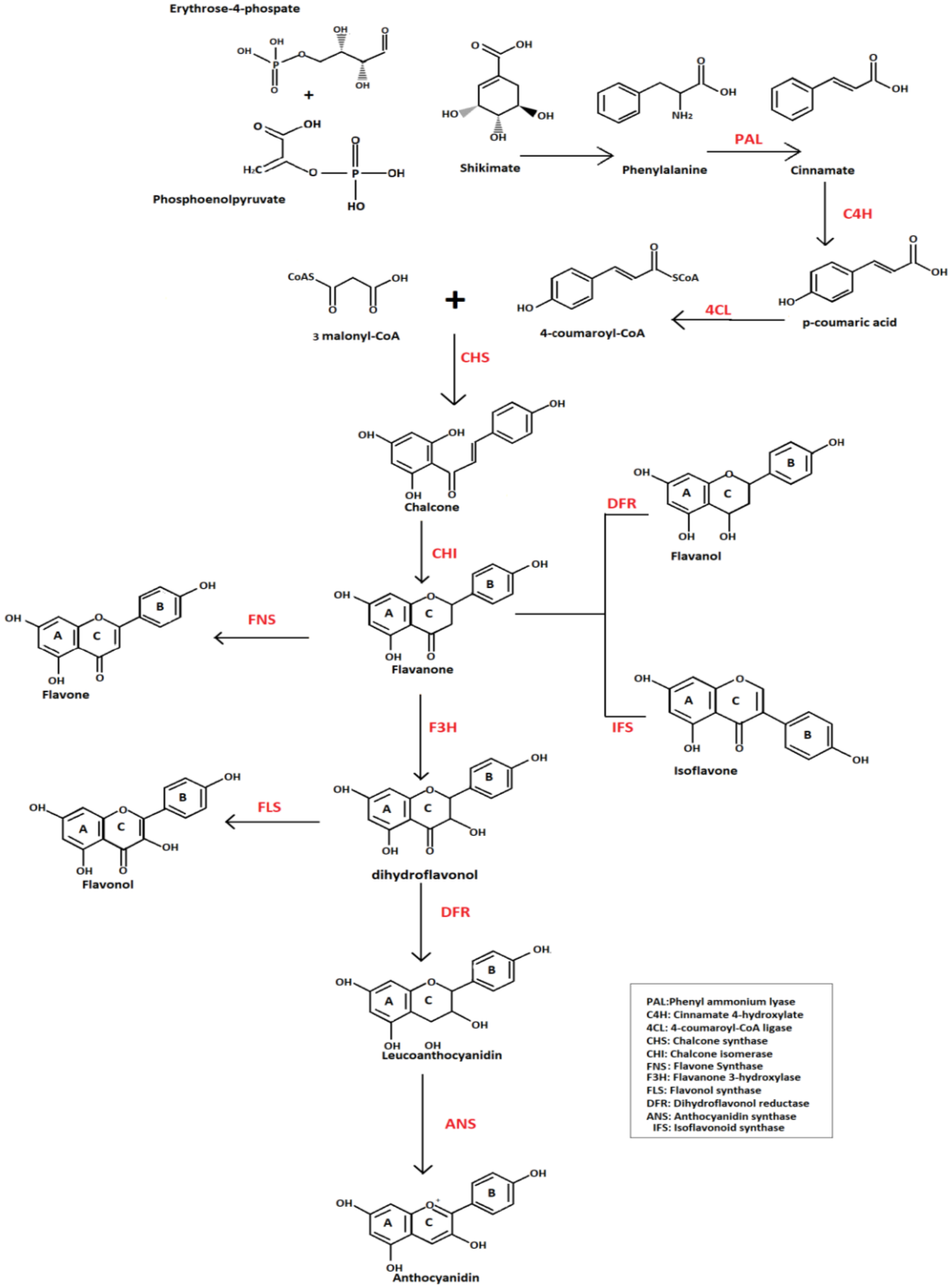
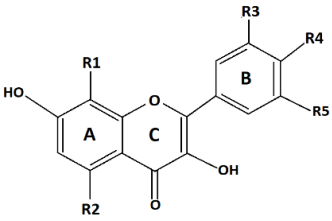


Figure 1. Biosynthesis of flavonoids.

2.1. Flavonols

Flavonols are the most abundant flavonoids in plants. The most studied subclasses of flavonols are the quercetins, kaempferols, myricetins and fisetins; distinctions in the structures of each subclass are shown in Figure 2. The substitution patterns in quercetins and kaempferols are 3,5,7,3′,4′-OH

and 3,5,7,4′-OH, respectively. These are very often found in plants as glycosides. The major dietary sources of flavonols are fruits and vegetables, predominantly onions, but also including the apple, strawberry, lettuce and other leafy vegetables. In addition, black and green tea and red wine are also rich sources of flavonols. In general, soft fruits, leaves of medicinal plants and green leafy vegetables have greater levels of flavonoids than other vegetable and fruit plants [20]. However, cooking may lower the concentration of flavonols in vegetables such as tomato and onion [21].



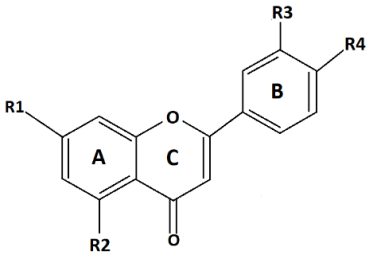
Flavonols

Subclass	R1	R2	R3	R4	R5
Kaempferol	H	OH	H	OH	H
Quercetin	H	OH	OH	OH	H
Myricetin	H	OH	OH	OH	OH

Figure 2. Flavonols: chemical structures, types and substitution positions in the basic skeleton.

2.2. Flavones

Flavones are one of the major subgroups of flavonoids. Fruits and vegetables including parsley, carrot, pepper, celery, olive oil, and peppermint are the main dietary sources of flavones [22]. Chrysin, apigenin, rutin (glycoside) and luteolin are the most studied subclasses of flavones. Substitution patterns in the basic structure of flavones are 5,7-OH (chrysin), 5,7,4′-OH (apigenin), and 5,7,3′,4′-OH (luteolin) [23] (Figure 3).



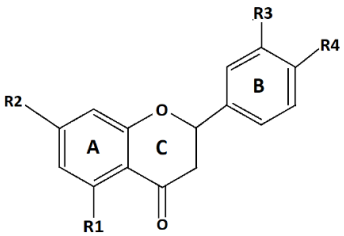
Subclass	R1	R2	R3	R4
Chrysin	OH	OH	H	H
Luteolin	OH	OH	OH	OH
Apigenin	OH	OH	H	OH

Flavones

Figure 3. Flavones: chemical structure, types and substitution positions in the basic skeleton.

2.3. Flavanones

Flavanones are different from flavones through their possession of a single bond between C2 and C3 of the C ring. Flavanones are most abundant in solid tissues of citrus fruits such as orange lemon and grape. The most studied types of flavanones are hesperidin and naringenin (Figure 4) The hydroxylation and substitution patterns in flavanone are 5,7,4′-OH (naringenin) and 5,3′-OH, 4′OMe, 7-rutinose (hesperidin) [23].



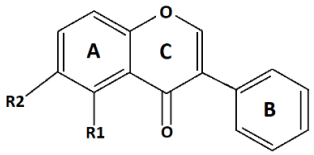
Flavonones

Subclass	R1	R2	R3	R4
Hesperitin	OH	OH	OH	O-Me
Naringenin	OH	OH	H	OH
Naringin	OH	O-Alk	H	OH

Figure 4. Flavonones: chemical structures, types and substitution positions in the basic skeleton.

2.4. Isoflavonoids

Isoflavonoids, with a B ring attached at 3-position of the C ring, are structurally different from other flavonoid classes. Isoflavonoids are found to be very helpful in microbial signaling and nodule induction in legume–rhizobia symbioses. Common examples of isoflavonoids are aglycone and glycosides of genistein and daidzein. The main natural sources of isoflavonoids are legumes such as soybean, as they are reported to exude these as signaling compounds to communicate with microbial symbionts [24]. The subclasses of isoflavonoids are shown in Figure 5.



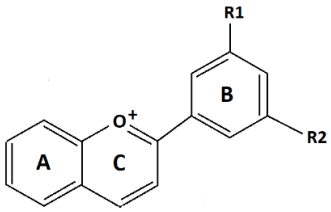
Isoflavonoids

Compound	R1	R2
Daidzein	H	H
Genistein	OH	H
Glycitein	H	OCH_3

Figure 5. Isoflavonoids: chemical structure, types and substitution positions in the basic skeleton.

2.5. Anthocyanidins

Anthocyanidins are responsible for the coloration of many fruits and vegetables. The red and blue colors in apple, grape and berries are due to anthocyanin or anthocyanin glycoside pigments [25]. The color depends on the structure of the compound which, usually changes due to hydroxylation and methylation at specific positions of the A and B rings [18]. Unlike other flavonoids, except flavanols, it carries no ketone group at the 4-position of C ring. Some of the anthocyanidin subclasses are shown in Figure 6.



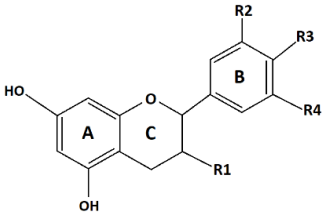
Anthocyanidins

Compound	R1	R2
Cyanidin	OH	H
Delphinidin	OH	OH
Pelargonidin`	H	H

Figure 6. Anthocyanidins: chemical structures, types and substitution positions in the basic skeleton.

2.6. Flavanols

Flavanols have a missing ketone group at the 4-position of the heterocyclic ring C, like anthocyanidins. The major sources of flavanols are grape (seed, pulp, stem and skin), berries, tea, wine, apple, pear and peach [26,27]. The most common examples of flavanols are (+)-catechin and (–)-epicatechin (Figure 7).



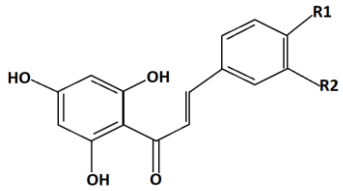
Flavanols

Compound	R1	R2	R3	R4
(+) Catechin	OH	OH	OH	H
(-) Epicatechin	OH	OH	OH	H
(-) Epigallocatechin	OH	OH	OH	OH

Figure 7. Flavanols: chemical structure, types and substitution positions in the basic skeleton.

2.7. Chalcones

Chalcone is the only class with an open ring; it serves as a precursor for various flavonoid classes. The missing C ring in the structure makes it quite different from other flavonoids. The major dietary sources of chalcones are apple, hops or beer [28], berries, tomato and certain wheats [18]. The most studied chalcone is chalco naringenin (Figure 8).



Chalcones

Compound	R1	R2
Naringenin chalcone	OH	H
Eriodictyol chalcone	OH	OH

Figure 8. Chalcones: chemical structure, types and substitution positions in the basic skeleton.

3. Role of Flavonoids in Plant Growth and Crop Yield

Plant growth and production are directly associated with soil productivity. In agronomic terms, it refers to the ability of soil to produce a certain yield of agricultural crops. However, the ability of soil is determined by numerous factors including soil physicochemical properties and management-related factors. Generally, it is the measure of inputs versus outputs, which in agronomic situations are related to water and nutrient supply (inputs) versus crop yield (output) [29]. In addition to these factors, the phytomicrobiome is becoming recognized as a key pillar and a major contributor to crop production. The soil is home to vast numbers of microbial species including free-living, symbionts, host-specific and non-host specific which could be either beneficial or harmful to plant growth and productivity. It is estimated that 1 g of soil contains 1 billion bacterial cells with 10,000 distinct genomes [30,31]. These microbial entities in phytomicrobial associations aid plants in their growth in both stressed and unstressed conditions, by a range of mechanisms. In the phytomicrobiome, associated entities trade for their benefits by aiding one another; microbes get reduced carbon-rich food materials exuded from plant roots and in turn, microbes aid plants in nutrient acquisition, disease resistance and stress mitigation by direct and indirect means. The contribution of the phytomicrobiome in relation to crop yield and production has been demonstrated by numerous studies [32–34]. However, this productive association is the result of crosstalk between trading partners, which is carried out by a complex signal cascade in the rhizosphere. In phytomicrobial associations, signaling is a key activity, and any interruption in signal transmission may disturb and/or reduce the interaction and efficacy of the symbionts.

Plants are equipped with biosynthetic machinery operating to supply thousands of bio-compounds that are required to perform vital functions. There is an array of compounds exuded from plant roots including sugars, amino acids, organic acids, phenolics, enzymes and growth regulators. These secretions serve as a source of carbon for many microorganisms associated with the plant root

system. Besides providing a carbon-rich environment, plants generate chemical signals: a mode of communication with microbes in the rhizosphere to initiate colonization and other specific activities for mutual benefit [35,36]. The changing environment and anthropogenic global warming, and demand for sustainable agriculture for future security, have increased the significance of the phytomicrobiome in agricultural practices. Research on this area is becoming more prevalent in the agricultural scientific literature, and scientists are working to better understand plant–microbial associations and signaling to increase their efficacy in order to obtain substantial yield enhancements. In this review, we considered publications highlighting plant-microbial association in relation to signal compounds: flavonoids affecting plant growth and their production. Flavonoids have direct and indirect positive impacts on plant growth and development. The production of specific flavonoids and their accumulation in certain plant tissues following external or internal stimulation is largely unexplained. However, flavonoids are very effective in certain plant–microbe interactions in the rhizosphere and can have effects in combating biotic and abiotic stresses [37]. The roles of flavonoids, flavonoid subclasses and substitution patterns are extensively demonstrated in Table 1.

Table 1. Flavonoid subclasses, dietary sources, major functions in plants and structural substitutions in the basic skeleton.

	Compound	Flavonoid Class	Structure Substitution	Food Sources	Role in Plants	References
1	Quercetin	Flavonols	3,5,7,3′,4′-OH	Onions, apples, berries	Antioxidant, Allelopathic	[38,39]
2	Kaempferol	Flavonols	3,5,7,4′-OH	Tea, broccoli, cabbage, beans, tomato, strawberries and grapes	Antioxidant, antibacterial, insect repellent, abiotic stress mitigation	[40–43]
3	Chrysin	Flavones	5,7-OH	Honey, propolis	Antioxidant, UV-A/B Resistance, AMF symbiosis	[40,44,45]
4	Apigenin	Flavones	5,7,4′-OH	Parsley, Pepper	Antioxidant, AMF spore germination (symbiosis), phytoalexin	[46,47]
5	Naringenin	Flavanone	5,7,4′-OH	Grape, apple, orange	AntioxidantAMF Hyphal growth (Symbiosis)	[25,48]
6	Hesperidin	Flavanone	5,3′-OH, 4′OMe, 7-rutinose	Citrus, orange juice	Antioxidant	[25,49]
7	Genistein	Isoflavonoid	5,7,4′-OH	Currants, raisin, legumes	Nodule induction, signaling	[24,46]
8	Daidzein	Isoflavonoid	7,4′-OH	Currants, raisin, legumes	Nodule induction, signaling, chelation	[46,50]
9	Apigeninidin	Anthocyanin	7,4′-OH	Flowers, fruits	Color pigmentation, pollinator attractant, UV-B absorber	[19,25,51]
10	Fisetin	Flavonols	3,7,4′,5′-OH	Apple, strawberry, onion, cucumber	Antioxidant	[25,52]
11	Myricetin	Flavonols	3,5,7,3′,4′,5′-OH	Berries, tea, wine	Antioxidant	[53]
12	Luteolin	Flavones	5,7,3′,4′-OH	Broccoli, chilli, onion leaves bilimbi fruit and leaves, carrot, local celery	*Nod* gene inducer	[54]
13	Rutin	Flavones	5,7,3′,4′-OH, 3-rutinose	Parsley, Pepper, carrot	Mycorrhizae symbiosis, abiotic stress mitigation	[22,55]
14	(+)-catechin	Flavanol	3,5,7,3′,5′-OH	Grapes, pears, apples	Antioxidant, ROS scavengers	[26,56,57]
15	(−)-epicatechin.	Flavanol	3,5,7,3′,5′-OH	Strawberry, apple	Antioxidant	[56,57]

3.1. Flavonoids in the Rhizosphere

The rhizosphere is the most complex and intensive place for the interaction of plants with the external environment. It is the area of maximum biological community activity, nutrient acquisition (mobility, solubility and diffusion) and plant–microbial interaction, which may depend on the secretion of exudates containing large and small molecular weight organic and inorganic compounds including ions, phenolics, enzymes, secondary metabolites and carbohydrates [58].

Flavonoids (secondary metabolites), very often in both aglycone and glycoside forms, are likely to be exuded from root systems and have indirect effects on plant growth by mediating belowground interactions, including attracting compatible rhizosphere-dwelling rhizobia, stimulating mycorrhizal growth and hyphal branching, enhancing solubility of nutrients including phosphorus and iron and repulsion of pests and root pathogens [50,59]. Studies suggested that flavonoid secretions from roots are carried out through active transport (ATP dependent), catalyzed by ABC transporters [60]. However, flavonoid secretion can also be passive, through degrading of root cap and epidermal cells [61]. In the rhizosphere, flavonoid persistence and mobility may be influenced by solubility, structure, availability of microbes and binding sites, as these compounds can be adsorbed to cation binding sites of soil or cell walls. Flavonoid glycosides are sparingly soluble in water and expected to be less adsorbed to binding sites, improving mobility and availability [10]. In addition, flavonoid secretion may be influenced by environmental stresses, including nutrient supply (nitrogen and phosphorus) in the soil [62].

3.2. Flavonoids and Legume-Rhizobium Interaction

The evolution of intimate relationships that enable plants and microbes to coexist has been the subject of many studies; these have attempted to explain and simplify the interactions that occur between an individual or specific plants and their symbionts. However, in reality, these interactions are far more complex and involve a range of microbes associated with a single plant, exchanging chemical signals [63]. However, these interactions aid plants in many ways. Soil fertility and/or nutrient acquisition is one of the major services provided by soil microbes. Nitrogen deficiency, due to rapid nitrogen loss from soil by leaching, denitrification and immobilization, is a leading problem in crop production. Atmospheric nitrogen is fixed and becomes part of the soil nitrogen recharge, by biological and artificial means, of fixation from the atmosphere. However, the natural biological fixation of atmospheric nitrogen (N_2) contributes about 60% of the total atmospheric nitrogen fixation, which has gained the attention of researchers and growers. Below-ground interactions leading to the establishment of legume nitrogen-fixing symbioses are carried out by signal exchange, as a mode of communication between host and symbiont, for mutual benefit.

The plants release chemo-attractants, in the form of flavonoids, to initiate the symbiotic process [64]. Flavonoids are very often exuded in greatest concentrations from root tips, which is near the site of rhizobium attachment and infection [65]. These secondary metabolites serve as signaling compounds to attract rhizobia toward plant roots and to activate *nod* genes in the rhizobia, which then start the nodulation process in legumes [66]. The *nod* genes are responsible for making lipo-chitooligosaccharides (LCOs), referred to as nod factors, which are released in response to chemical stimulus (generally isoflavonoids) from plant roots. LCOs or other nod factors initiate root hair curling, the formation of infection threads and bacterial entrance into the host plant root cells [67]. In legume crops, almost half of the nitrogen required is fixed by nitrogen-fixing microbes, predominantly, *Rhizobium* and *Bradyrhizobium*; the rest is supplied by fertilizer supplements [68].

Isoflavones are considered to be very active and effective in plant–microbe interactions; they are very operative in signaling and enhancing nodulation by inducing *nod* gene systems. *Nod* gene inducing flavonoids (quercetin and luteolin) released from the seeds and roots of *Medicago sativa* L were investigated. Many, but not all, of the flavonoids, were found to induce *nod* genes in *Rhizobium melioti* [69], indicating that rhizobia is responsive to selective flavonoid signals. Nodulation related gene induction in *R. melioti* by flavonoids released from alfalfa was investigated. A chalcone (4,4′-dihydroxy-2′-methoxychalcone) released, was reported to be the primary *nod* gene inducer in the

group. Moderate inducing activities for 4′,7-dihydroxyflavone and 4′-7-dihydroxyflavanone were also reported [70]. In addition, genistein (isoflavonoid), was tested under salt stress with inoculation of *Bradyrhizobium* to evaluate effects on nodulation, N_2-fixation and physiological changes. The results revealed that genistein increased photosynthesis levels, nodulation and nitrogen fixation under saline and non-saline conditions [71]. Isoflavonoids are hypothesized to induce *nod* gene expression and to control the concentration of auxin in soybean roots. Results from similar work provided genetic evidence of isoflavonoid involvement in soybean nodulation and assumed this to be essential for nodule induction, by inducing the *nod* genes in *Bradyrhizobium japonicum* [72].

These biological signals are crucial factors in plant–microbe associations and are very often disrupted by known and unknown causes. Studies on subtropical legume (soybean) nodulation indicated that root zone temperatures (RZTs) below 25 °C decrease nodule induction and N_2-fixation [73,74]. The appropriate range of RZT required for optimal nodulation is 25 to 30 °C. Below optimal RZT (25 °C), with each degree decrease in temperature there is a 2-day delay in the onset of N_2-fixation; below 17 °C each degree RZT decrease delays the onset of N_2-fixation by about one week [75]. However, suboptimal RZTs hinder root hair infection to a greater degree than nodule initiation and development [76]. In addition, N_2-fixation activity by the nitrogenase enzyme complex is delayed, as is nitrogen assimilation [77]. However, the interorganismal signaling disruption by suboptimal RZTs (17.5 and 15 °C) could be minimized by genistein application. Preincubation of *Bradyrhizobium japonicum* with genistein increased the number of nodules, N_2-fixation and plant total dry weight at suboptimal RZT. It is, at least in part, because rhizobial *nod* gene induction is temperature-dependent, making bradyrhizobia less sensitive to signal molecules. However, nodulation events began earlier at suboptimal RZT following genistein application and this stimulated the production of nod factors (LCO), nodule formation and nitrogen fixation [78].

The environmental growth conditions, in terms of nodulation and N_2-fixation, may affect the efficacy of applied signaling compounds and/or inoculated microbial strain, for example, under field conditions, the plant root system is surrounded by an array of phytomicrobiome members, which may compete for plant-supplied reduced carbon; in addition, other factors such as temperature, CO_2 limitation, water and nutrient supply may alter nodulation and the onset of nitrogen fixation [79,80]. However, similar results were observed by preincubation of *B. Japonicum* with genistein application under field conditions. Genistein application improved N_2-fixation (40%) and total nitrogen yield through increased nodule numbers and accelerated onset of N_2-fixation; however, these effects were greater in N-stressed plants. In addition, genistein preincubation of *B. japonicum* has meaningful impacts on yield components [81]. Genistein preincubated inoculum (*B. japonicum*) increased soybean grain yield and protein content by 16 and 70% respectively, as compared to those receiving only inoculum [82]. Similar studies indicated an increase in yield and protein content of soybean by 25.5 and 21.6%, respectively [78]. However, crop responses to genistein application vary with the genetic makeup of the crop cultivars. It was suggested that high yield potential cultivars respond more to genistein application [83]. In addition to crop responses, the cultivar differences also determine the concentration and accumulation of a range of secondary metabolites. The influences of soybean cultivars and selection for yield on the concentration of health beneficial compounds, including isoflavonoids (examples being genistein and daidzein) were determined. The findings revealed a positive correlation between yield and isoflavonoid concentration and suggested that breeders selecting for higher soybean yield may select for higher isoflavonoid concentration. However, isoflavonoid concentrations were negatively correlated with protein content, unlike oil content [84].

3.3. Flavonoids and Mycorrhizal Associations

Phosphorus (P) is the second most important plant nutrient, after nitrogen. However, P is one of the most deficient and least accessible primary nutrients and is often limiting to plant growth. Phosphorus solubilization and affinity for the soil matrix and organic complexes are crucial reasons for its unavailability for plant utilization. The rhizospheric microbial community plays a vital role in

phosphorus availability and solubility by producing enzymes that can mobilize adsorbed phosphorus and enhance the process of mineralization. Moreover, beneficial soil microbial species have positive impacts on root growth and development and may increase root surface area, which ultimately enhances the phosphorus depletion zone and effective phosphorus mobility [85]. In plant–mycorrhizal symbioses, mycorrhizal fungi regulate plants to reduce root growth while increasing root extension through hyphal outgrowth (100 times longer than root hairs) and the depletion zone for phosphorus, increasing its availability by extending and proliferating in the soil far beyond the reach of root surfaces [86]. Arbuscular mycorrhizal (AM) associations are probably the most taxonomically extensive associations, formed by 70–90% of plant species. Arbuscular mycorrhizal associations are formed by a monophyletic group of fungi from the phylum Glomeromycota which is estimated to utilize about 20% of plant photosynthates, which is approximately equal to 5 billion t of carbon per year [87]. The mycorrhizal symbiosis is very effective at enhancing plant growth in drought conditions and nutrient-deficient soils, specifically those that are phosphorus-deficient. It was observed that AM inoculation increased potato yield by 9.5% in inoculated fields, as compared to uninoculated fields, with yields of 42.2 and 38.3 t ha^{-1}, respectively. Arbuscular mycorrhizal associations have substantial potential to increase crop productivity, but their efficacy and association in large-scale crop production systems are not yet fully investigated [34].

Root exudation, chemo-stimulation and presence of other microbial communities in the rhizosphere may affect mycorrhizal symbioses and their colonization. Root exuded flavonoids have been shown to enhance the mycorrhizal symbioses by stimulating fungal spore germination, hyphal growth and colonization of roots. Flavonoids are considered to be universal signaling compounds [88]. However, some scientists have a different perception regarding AM symbiotic signaling. The normal development of mycorrhizal relationships in the absence of flavonoid-based signaling compounds in carrot root extracts and deficient activity of chalcone synthase (necessary for flavonoid biosynthesis) brought them to a conclusion that "Flavonoids are not necessary plant signal compounds in Arbuscular Mycorrhizal symbiosis". However, if present, their influence greatly stimulates AM development [89] and plant growth depending on concentration, spore density and plant growth stage [90].

The effects of the AM stimulating flavonoid, formononetin, on potato yield mediated by native AMF were examined. The results revealed an increase in plant dry matter, tuber development and phosphorus use efficiency. Perhaps the effects were more prominent at low phosphorus (P) levels. In addition, formononetin increased soil sporulation more than 3 fold [91]. However, the variation in response of different cultivars to formononetin application indicated that signaling responses by participatory symbionts may depend on genetic characteristics [92]. Similar results suggested that formononetin seed application to soybean may reduce the need for phosphorus (P) fertilizer by 50% [93]. A similar study was conducted on the hyphal growth and root colonization of arbuscular mycorrhizal fungi (AMF) on tomato as affected by flavones and flavonols. A correlation was observed between the number of entry points and root colonization percentage for the specific tested AMF (*Gigaspora rosea*, *Gigaspora margarita*, *Glomus mosseae*, and *Glomus intraradices*). Flavones (chrysin and luteolin) and flavonols (morin) enhanced the colonization and number of entry points, whereas kaempferol and rutin have no effect on presymbiotic growth of AMF and subsequent root colonization [94]. The flavonoids (apigenin, hesperetin and naringenin) enhanced spore germination, hyphal growth and root colonization of *Gigaspora margarita* [95]. In addition, quercetin glycosides, exuded from alfalfa, were found to be effective in enhancing AMF symbioses by increasing hyphal growth and branching, and spore germination of *G. macrocarpum* and *G. etunicatum* [50].

Moreover, flavonoids have been found to solubilize phosphorus by enhancing mycorrhizal colonization of root systems and may help in nutrient availability and mineralization of nitrogen and other nutrients [96]. They may also act as metal chelating agents, making certain micronutrients more available for plants [97]. Flavonoids released from roots of white lupin cause significant increases in phosphorus acquisition [98]. An Isoflavonoid present in root exudates of alfalfa was shown to dissolve phosphates of iron, making both iron and phosphorus more available to plants. In addition, flavonoids,

including genistein, quercetin and kaempferol, can make iron available by chelating and reducing iron oxides in the rhizosphere from Fe^{+3} to Fe^{+2} [99].

4. Flavonoids and Plant Abiotic Stresses

Plants, as they are sessile, are exposed to an array of unfavorable environmental conditions. Ecological variations and intense growth conditions affect plant hemostasis, physiology and growth, leading to diminished and stunted plants. A wide range of unfavorable biotic and abiotic stresses threaten sustainable agriculture and are often responsible for diminished crop production [100]. The mechanisms plants use to cope with abiotic stresses are coordinated among plant organs and tissues through chemical signals [101]. Most plant responses to stress conditions are not fully understood. However, the biosynthetic flavonoids and their ability to induce resistance against biotic and abiotic stresses have acquired some attention. Flavonoids are found to be supportive in abiotic stresses, including UV radiation, salt and drought stress.

4.1. Flavonoids as UV Scavengers

UV radiation is invisible, short wavelength and highly energetic radiation. UV radiation is divided into three segments based on the wavelength of the light: UV-A, B and C with a wavelength of 315–400 nm, 280–315 nm and less than 280 nm, respectively [19]. These wavelengths have enough energy to cause damage and abnormalities in plants by breaking chemical bonds through photochemical reactions [62]. The energy of the photon depends on the wavelength of the radiation; the shorter the wavelength, the more energetic the radiation will be. UV-C (less than 280 nm) is most energetic and can ionize certain molecules. UV-B can cause severe metabolic disruption in plants by negatively affecting photosynthesis, starch concentration and transpiration, and promoting cellular damage; it may also increase disease susceptibility by making defense mechanisms weak, affecting the process of cell division and inhibiting overall plant growth [65,102,103]. However, the absorbance of UV-B radiation by flavonoids permits little radiation in this wavelength range to pass through leaf epidermal cells [62]. Plant resistance to UV radiation is due to flavonoids (anthocyanins) filtering UV-B by absorbing such radiations and detoxifying the ROS produced by photochemical reactions [104].

The significance of UV-B scavenging flavonoids on two apple varieties (Granny Smith and Braeburn) exposed to sunlight and UV-B radiation was estimated. The results revealed different contents and compositions of UV-B absorbing compounds in the two varieties. The Granny Smith (anthocyanin-free) fruit showed significant decreases in chlorophyll and carotenoid contents. Conversely, Braeburn exposed to sunlight had higher contents of chlorophyll and carotenoids. However, quercetin glycosides were the principal compounds absorbing UV-A and UV-B radiations. [105]. Similar work has investigated tomato under controlled environment conditions; the findings demonstrated an increase of flower/fruit synchronization under high radiation, with minimal effect on vegetative plant parts. In addition, an increase of UV-B receptors and chlorophyll content was also observed, along with phenylpropanoid compounds responsible for UV absorption by-products of antioxidant pathways. [106]. UV-A/B, as an abiotic stress, can be used to enhance fruit quality by activating oxidation pathways in plants [107].

The effect of UV light on flavonoid content in barley leaves was tested, and results revealed significant increases in flavonoid (saponarin, lutonarin) content when leaves were exposed to UV-B radiation, as compared to control conditions (absence of UV-B) [108]. In addition, the increased flavonoid accumulation in response to UV-B radiation may reduce the damage in exposed leaves by absorbing specific radiation wavelengths. [109]. Therefore, plants grown in open-environment conditions, exposed to full sunlight, have greater flavonoid contents than plants grown in greenhouses.

4.2. Flavonoids in Managing Salt and Drought Stress

Salinity, one of the most concerning abiotic stressors, is a major constraint to global crop productivity. The worldwide extent of soil affected by salts is about 955 M ha, while 77 M ha are

affected with secondary salinization, and of these 58% are irrigated lands. Almost 20% of irrigated land is affected by excess soluble salts [110]. Soil salinization and increased accumulation of soluble salts in the root zone, predominantly NaCl, is caused by natural and/or human activities which have resulted in degraded and abandoned formally fertile and productive agriculture lands [111]. Excess soluble salts in soil solution may limit plant growth, primarily through two mechanisms: osmotic stress and ion toxicity. First, low solute/osmotic potential due to increased ion concentration (NaCl) in soil water reduces the total soil-water potential (Ψ) which in turn reduces the ability of plant roots to uptake water, eventually leading to diminished plant growth. Second, ion toxicity in plant tissues, more frequently due to sodium accumulation, causes cellular damage by membrane disruption and disturbs plant physiological processes, including photosynthesis, respiration, transpiration and osmoregulation, resulting in necrosis or chlorosis, leading to reduced plant growth [112–114]. Depending on sensitivity and tolerance to salinity, plants are classified as either glycophytes or halophytes [115]. Most of the agricultural crops are glycophytes (low tolerance) and tend to exclude Na^+ and Cl^- from roots. Unlike glycophytes, halophytes are often native to saline growth conditions and tolerate salt concentrations that kill 99% of other vegetation. The salinity tolerance of halophytes relies on ionic homeostasis by controlled uptake and compartmentalization of ions (Na^+, K^+, and Cl^-) and accumulation of metabolically compatible solutes (organic) in the cytoplasm to balance the solute potential of ions accumulated in the vacuole [116,117]. Salt responses in plants follow a biphasic mechanism. The first, osmotic phase (rapid), begins immediately after root zone salinization increases to a threshold level, resulting in reduced shoot growth and leaf area, and causes stomatal closure. The second, ionic phase, begins with increased accumulation of ions (Na^+) to toxic levels in the cytoplasm, leading to chlorosis followed by leaf death. Osmotic stress not only exerts immediate effects on plant growth but is also more chronic than the ionic phase [118]. Increases in an array of compatible organic solutes is proposed to balance solute potential including sucrose, proline, glycine-betaine and sorbitol [119,120]. In addition to compartmentalization, some plants can prevent salt accumulation (whole plant or cellular level) and avoid toxic effects of ions on crop physiology including photosynthesis [113]. In response to salt stress, plants undergo several morphological, physiological and metabolic changes to cope with the stress conditions. These adaptations involve several biochemical pathways, sustained osmotic potential, ion compartmentalization and exclusion of toxin ions. Subsequent to ionic toxicity, specific toxic substances, ROS, including superoxide, singlet oxygen and hydrogen peroxide, cause oxidative damage in cells, which is considered a secondary effect of salinity [121,122]. However, plants are equipped with specific defense mechanisms to cope with such stress conditions, by initiating antioxidant pathways including enzymes and antioxidant agents; flavonoids, carotenoids and specific vitamins [121,123,124]. Reactive oxygen species or free radicals are molecular species that contain at least one unpaired electron in their atomic shells, making them highly reactive. Reactive species (RS) are quite unstable, most of them exist not more than 10^{-6} s in biological systems, and to be more stable they react with biomolecules by either donating or receiving an electron [125].

Oxygen is poisonous; aerobes are equipped with defense mechanisms mediated by antioxidants, which is how they survive such toxicity. The antioxidant defenses in biological systems are the result of several strategies [126]:

1. Suppressing RS formation either by uncoupling proteins triggered by superoxide, indicating that it may reduce mitochondrial ROS formation [127] or inhibition of enzymes involved in RS formation, for example, inhibition of cyclooxygenase, lipoxygenase and NADH oxidase by flavonoids [128]
2. Substitution of biomolecules vulnerable to oxidative damage with resistant ones
3. Antioxidants acting as "sacrificial agents" by reacting with reactive species to prevent them from reacting with important biomolecules [129].

Flavonoids have been found to play an important role as antioxidants by detoxifying and scavenging of ROS produced [130] as by-products of oxidative metabolism [121] during abiotic stresses

including salt and drought. However, the accumulation of such metabolites advances when plants face any environmental uncertainty. It was observed that anthocyanin accumulation in response to salt stress increased by 40%, which could be a phytochemical strategy to combat salt stress and subsequent toxic reactions [131]. In addition, the protective nature of anthocyanin was also compared in two groups of rice genotypes: salt sensitive and salt resistant. The total anthocyanin content in salt-tolerant genotypes was higher than in salt-sensitive varieties, with antioxidant activities of 125–199% and 106–113%, respectively. It was therefore concluded that anthocyanins in rice contribute to cellular protection by detoxifying accumulated salts [132]. The effects of applying genistein (an isoflavonoid) to rhizobial culture on signal production and subsequent growth and yield of soybean have been investigated. Results demonstrated a significant increase in plant growth with increased leaf area and number of nodules. Genistein application enhanced crop yield by 21% under salt stress [133]. Salinity may inhibit signal exchange between host and symbiont, which is very important for initiating a functional symbiotic nitrogen-fixation relationship. The interaction of soybean and *B. japonicum* was evaluated under salt stress. The findings are consistent with similar studies. Genistein application enhanced the stimulation of growth and signaling between the symbiotic partners and, hence, increased nodulation and growth of the plant. The results may help in cultivating soybean in a more efficient and productive way under unfavorable environmental conditions [134]. Likewise, an increased concentration of flavonoids has been found in tomato plants when exposed to salt or drought stress, however, plant growth and chlorophyll content were significantly reduced, indicating no and/or insignificant effect of flavonoids on plant growth and physiology [121]. In contrast, findings from a similar study on flavonoid biosynthesis and accumulation in wheat leaves under drought stress suggested that drought resistance in wheat is closely related to increased flavonoid accumulation [135]. Similar results were observed in two native shrubs from Argentina. Flavonoid accumulation was observed throughout the year; however, a significant increase was noted during times of intensive drought [136]. Drought mitigation by flavonoids and flavonoid derivatives has been confirmed in *Arabidopsis thaliana*. The role of individual flavonoids was unclear, however, increased production of flavonoids in plants and associated drought resistance was confirmed [95].

5. Flavonoids against Plant Biotic Stress

Plants, as they are sessile, have no possible way to physically remove themselves from invading pests and pathogens. In nature, plants are exposed to an array of pathogenic fungi, bacteria and herbivore pests. However, plants have evolved strategies to combat such unwanted guests. Pathogens do not generally succeed in infecting plants that are not host species (non-host resistance) and/or resistant varieties (incompatible interaction), but intense damage after infection may be caused in susceptible plants (compatible). The damage caused by pathogens in most cases is inversely correlated with the hypersensitive response including reinforcement of cell wall, induction of lytic enzymes and production of phytoalexins [137]. One of the defense strategies adopted by plants in response to invading pests and pathogens is formation, accumulation and secretion of phytoalexins. Phytoalexins are chemicals released by plants in response to pests and pathogens, to ward off the disease and disease-causing agents. Flavonoids are the most-described secondary metabolites in plant defense systems [132]. Their role in plant physiology, morphology and communication and defense mechanisms is considerable. Certain flavonoids are found to be strong phytoalexins against pathogenic bacteria, fungi and nematodes, and may act as insect repellents. External morphological modifications in plants may also act as protective mechanisms against invading pests, predominantly feeding animals including insects, however the chemical tool of insect repellent is more effective. The synthesis of these antibiotic secondary metabolites in plants is due to infection caused by pathogens, bacteria, fungi and nematodes, and may also be induced by feeding insects [138,139].

5.1. Phytoalexin Flavonoids as Nematicides

Parasitic nematodes cause tremendous crop yield loss by forming cysts or galls on roots. Plants, in response to nematode invasion, produce several chemicals to increase resistance to or minimize the effect of, nematode presence. The synthesis and accumulation of flavonoids within plant root systems is often stimulated by nematode invasion. The induced synthesis of such phytoalexins assists plants in coping with nematode infections.

Coumestrol (an isoflavonoid) can act as a phytoalexin; it is synthesized in lima bean as nematicide when infected by *Pratylenchus penetrans*. Glyceollin is a protecting isoflavonoid synthesized in soybean roots when infected by the root-knot nematode; *Meloidogyne incognita.* The results demonstrated a decrease in nematode mobility and O_2 uptake [140]. The synthesis of glyceollin, resistance inducing flavonoids in soybean, in response to *Meloidogyne penetrans* infection minimized crop damage [141]. *Heterodera glycines* (soybean cyst nematode) is the most destructive parasitic nematode of soybean. Accumulation of the phytoalexin glyceollin in root systems of soybean after cyst nematode invasion was determined by HPLC (High Performance Liquid Chromatography): A form of liquid chromatography, used to separate, identify and quantify compounds in a solution. No glyceollin was found in control plants, however, the content of the phytoalexin glyceollin increased at the 2^{nd}, 4^{th} and 6^{th} days after inoculation, by 12, 19 and 23 μg g^{-1} root, respectively [142]. The major phytoalexin in oat, when infected with major nematodes of cereals, was identified as O-methyl-apigenin-C-deoxyhexoside-O-hexoside (a flavone-C-glycoside). The phytoalexin flavone, induced by nematode invasion, was extracted from oat roots and shoots, and was significantly reduced invasion by major cereal nematodes: *H. avenae* and *P. neglectus* [143]. The interaction of flavonoids with parasitic nematodes as defense mechanisms is unclear, however, flavonoids were found to be protecting agents as they inhibit nematode motility and chemotaxis [140].

5.2. Flavonoids against Pathogenic Fungi

Fungi, as the most dominant disease-causing agent in plants, adversely affect agricultural crop production. The wide range of diseases caused by fungi decreases crop production dramatically. However, plants have adapted themselves to produce resistance mechanisms against biotic stresses. The production of phytoalexins in response to pathogenic invasion, predominantly fungi, is an effective tool used by plants for combatting biotic stress. The effect of cucumber powdery mildew and subsequent biochemical changes in response to invading pathogen was investigated. Results revealed that silicon can contribute to powdery mildew resistance in cucumber by increasing the accumulation of a fungi-toxic phytoalexin, which was identified as the flavonol aglycone rhamnetin (a flavonoid) [144]. Brown rot lesion is a disease caused by the fungus *Phytophthora citrophthora* in citrus fruits. The correlation of infection caused by pathogen and level of phytoalexin flavones accumulation in host plant was examined. The increased accumulation of heptamethoxyflavone, nobiletin, sinensetin, and tangeretin was confirmed along with the antifungal effects of phytoalexin flavonoids. The most effective flavonoids against *P. citrophthora* were naringenin and hesperetin [145]. Similar results were found in tangelo fruit defense mechanisms against *P. citrophthora.* The accumulation of isoflavonoids was induced by 6-benzylaminopurine application, which enhanced fruit resistance to the pathogenic fungus by 60%. The most inhibiting of the accumulated phytoalexins were nobiletin, sinensetin, heptamethoxyflavone, followed by tangeretin [146]. Further research was carried out to evaluate phytoalexin accumulation in soybean cotyledons using four species of *Aspergillus.* All the pathogenic species induced accumulation of phytoalexins in soybean cotyledons, however the phytoalexins glyceollin at 955 μg g^{-1} (fw) and coumestrol at 27.2 μg g^{-1} (fw), following inoculation with *A. sojae* and *A. niger*, accumulated to the greatest degrees [147].

5.3. Antibacterial Effects of Flavonoids

The study of natural defense mechanisms of plants related to synthesizing antimicrobial phytoalexins in response to biotic stress demonstrated that phytoalexin level is increased as part of the resistance to phytopathogenic agents [148]. Information regarding phytoalexin accumulation in response to fungal invasion is considerable, however very little is known about phytoalexin synthesis in response to phytopathogenic bacterial invasion [149]. The production of antibacterial phytoalexins in bean leaves was studied by inoculating bean plants with *Pseudomonas spp.* Coumestrol, a phytoalexin isoflavonoid, was accumulated in infected bean leaves and inhibited the growth of two pathogenic bacterial species: *P. mars-prunorum and P. phaseolicola*. The coumestrol was obtained from hypersensitive and susceptible lesions at 1 and 5 days after inoculation. Their accumulation explains the inhibition of bacterial colonization in hypersensitive and susceptible lesions of bean leaves [150]. The accumulation of isoflavonoid in soybean leaves in response to *Pseudomonas glycinea* invasion was investigated. Coumestrol and daidzein were identified as the major phytoalexins accumulated in response to pathogenic (*P. glycinea*) and non-pathogenic (*P. lachrymans*) inoculations of soybean leaves. The data demonstrated inhibiting properties of coumestrol against pathogenic bacterial colonization and suggested that the resistance in soybean leaves against *P. glycinea* was due to induced accumulation of isoflavonoids [151]. In contrast, coumestrol was found ineffective against pathogenic bacterial strains when tested with another five isoflavonoids on twenty isolates of pathogenic and saprophytic bacteria, including species of *Pseudomonas, Xanthomonas* and *Achromobacter.* However, phaseollinisoflavan and kievitone showed antibacterial activity by strongly inhibiting the population of *Xanthomonas* and *Achromobacter* species [152]. Recent research toward finding natural solutions against biotic stress introduced new products against certain disease-causing agents. A new compound isolated from the roots of *Erythrina poeppigiana*, identified as an isoflavonoid was isolated against *Staphylococcus aureus,* and compared with five other root isolates. Results revealed strong inhibiting activities against inoculated pathogens. The minimum inhibitory concentration was 12.5 g mL^{-1} against thirteen (13) strains of S. *aureus.* It was also assumed that new compounds could act as potent antibiotics against infections caused by *S. aureus* [153].

5.4. Flavonoids as Insect/Herbivore Repellents

Plants, as sessile beings, act as an available food source for herbivores, including insect pests. Plants have evolved defense strategies to avoid and/or deal with such biotic stresses, by secreting and accumulating repellent molecules or signals, which are either plant constitutes, in some cases produced inductively in response to pest invasion [154]. The defense mechanism may initiate from undamaged tissues by secreting phytoalexins in response to chemical signals from wounded tissues, which may repel or intoxicate insects [155]. Most of the insect repellent or antifeedant molecules are alkaloids, flavonoids and other secondary metabolites [156]. Morphological modifications like thorns and waxes can make feeding difficult for insect pests. Plants usually use two different strategies: direct and indirect methods, as defense mechanisms against insect herbivory. Direct methods involve the accumulation of insect repellents or toxic substances to minimize the level of damage. On the other hand, plants release signaling compounds as chemoattractants to signal predators, which may feed on the pest and minimize the plant damage [157]. Rotenone (isoflavonoid) is a very effective botanical insecticide used as a basis for insect repellents. Rotenone is a major component of insecticidal resins which may be extracted from roots of some legumes, including those in the genera *Lonchocarpus, Derris* and *Tephrosia*. Pyrethrum is another bioactive material against insect pests, also containing flavonoids as a major constituent. Pyrethrum can be extracted from flowers of *Chrysanthemum* species [158]. Likewise, the antifeeding effects of four isoflavonoids (genistein, formononetin, daidzein and biochanin A), isolated from two red clover cultivars, were investigated against clover root borer. The isoflavonoids decreased insect weight and activity. Genistein and formononetin had high anti-feeding activity against *Hylastinus obscurus* (clover root borer). The results could be utilized in controlling curculionid [159]. In addition, the insecticidal effects of phenolics of pea plants were tested against *Acyrthosiphon pisum.* The high

concentration of phenolics and flavonoids in infested plants, as compared to controls, suggested the induced accumulation of antifeedants in response to insect pest presence. In addition, flavonoids (luteolin and genistein) added as supplements to artificial diets prolonged the stylet probing, onset of salivation and passive ingestion. Salivation and passive ingestion completely stopped at higher concentrations of flavonoids. such measures could be employed to induce resistance against certain invading pests [160]. Additionally, the role of phenolics and flavonoids as insect repellents is illustrated by several lines of research [161–163]

The antifeedant and toxic effects of four isolated flavonoids (isoglabratephrin (þ)-glabratephrin, tephroapollin-F and lanceolatin-A) from aerial parts of *Tephrosia apollinea L.* were determined. The flavonoids exhibited toxic effects against insect pests: *Sitophilus oryzae, Rhyzopertha dominica* and *Tribolium*, with mortality percentages of 78.6, 64.6 and 60.7%, respectively, at 3.5 mg mL^{-1}. [164]

6. Allelopathic/Phytotoxic Behavior of Flavonoids

Weeds are a very significant challenge to crop plants as they are constantly competing for light, nutrients and water, interfering with crop functioning and causing tremendous yield loss directly or indirectly. Reductions in crop yield are generally much greater due to weeds than other pests. It is estimated that about 34% of yield loss among the major crops is caused by weeds [165]. Some of the major crops affected by weeds are wheat, soybean, rice, maize, cotton and potato with yield reductions of 23, 37, 37, 40, 36 and 30% respectively [166]. Weed management strategies have always been a significant part of agricultural systems but have changed significantly based on the accessibility of tools and techniques, environmental and sustainability concerns, starting from ancient techniques such as pulling by hand and soil tilling with simple tools, to current use of herbicides and mechanized conventional tillage, which are the most recent and, so far, most effective techniques available [167]. However, despite being very effective, commercial herbicides are finding themselves eschewed by growers because of their toxic and residual effects which contravene the principles of sustainability, eventually contributing to climate change, which is a consequence of such unsustainable human activities. In addition, the continuous use of chemical herbicides induces herbicide resistance in weed populations, which is a crucial long-term consideration in weed management. In contrast, biopesticides are gaining significant popularity among crop scientists because of their environmentally friendly behavior, as they contain biochemicals with no, or minimal, residual effects. The concept of using plant-derived biochemicals as "weedicides" originated from the allelopathic effects mediated by certain plants by employing allelochemicals released into the environment.

The term allelopathy was first defined by Molisch [168], indicating that the effects that result (directly or indirectly) from exuded biochemicals transferred from one plant to another. This definition, suggested by Molisch, implies only plant activity. However, the term "allelopathy" was later refined to include microorganisms (bacteria, algae, fungi and viruses) in his definition, as a significant part of allelopathic processes [169]. Allelopathy is an interference process in which either plants or their dead parts exude phytotoxic chemicals which interfere with the physiology and growth of other plants [170]. The allelopathic behavior of certain entities (plants and microorganisms) has been demonstrated in the literature, however, given the extensive uncertainty, this area needs more exploration in order to understand allelochemical behavior, including the formation of allelopathic compounds and their chemical nature, viability, efficiency and mode of action in plant-plant and plant–microbe interactions, to improve their practical implementation in the field.

Several plants are known to have allelopathic natures through allelochemical exudation including wheat, rice, rye, barley, sorghum and sugarcane. These plants can be manipulated to suppress weeds through an allelopathic approach within crop rotations, intercropping, cover crops and mulch [171]. The phytotoxic effect of sunflower cultivars was evaluated against weed species in wheat either by growing with weeds or applied as residues over a wheat crop and weeds. Sunflower cultivars have shown strong allelopathic effects on weeds, however, variation among the cultivars was observed, indicating that allelochemical exudation or phytotoxic effects and weed suppression vary with cultivar/genotype.

In addition, the sunflower cultivars suppressed total weed density and biomass by 10–87% and 34–81%, respectively [172].

There is an array of biochemicals, produced as secondary metabolites in plants, or released during their decomposition by microbes, which act as active allelochemicals in plant ecosystems. These phytotoxic substances, based on their chemical nature, are classified into 14 categories including cinnamic acid and its derivatives: coumarin, flavonoids, tannins, terpenoids and steroids. Recent publications regarding flavonoids have evidenced their phytotoxicity and growth inhibitory effects, which could be a sustainable approach toward integrated weed management [173].

In early plants, bryophytes and ferns, some of the allelochemicals found are synthesized in the early stages of flavonoid biosynthesis, however, additional flavonoid classes accumulate in angiosperms and gymnosperms, reflecting the employment of genes beyond just those involved in flavonoid biosynthesis [137]. Flavonoids have been reported in the literature for over 50 years as allelochemicals in the rhizosphere [174]. They are either exuded from roots or released from decomposed plant tissues as leachates, persist for days in the soil and their activity (inhibitory or stimulatory) depends on their concentration and solubility. In addition, phytotoxic compounds can also accumulate in leaves and pollen, which eventually inhibit seed germination of other plants after falling onto the soil [12].

It has been observed that flavonoids are produced by many legumes; quercetin and kaempferol (aglycon and glycosylated) released from seeds and roots, possess phyto-inhibitory effects. If present in lower concentrations such compounds may stimulate seed germination while in higher concentrations they may inhibit seedling growth [175]. Flavonoids isolated from roots of *Stellera chamaejasme* L., a toxic and ecologically threatening weed, showed strong phytotoxic activity against *Arabidopsis thaliana*. The isolated flavonoids reduced seedling growth and root development. In addition, endogenous auxin distribution in *Arabidopsis thaliana* was also influenced, indicating a critical factor in phytotoxicity [176]. Spotted knapweed is one of the more noxious and economically devastating weeds of North America, destroying crops and other weeds by phytotoxicity. An allelochemical identified was flavan-3-ol (¬-)-catechin (flavonoid), was shown to be responsible for the invasive behavior and phytotoxicity of *Centaurea maculosa* (spotted knapweed) [103].

Recently, the herbicidal effects of 10 crude extracts obtained from Tunisian plants were assessed. Among the five phenolic compounds, three of the flavonoids had significant herbicidal effects on *Trifolium incarnatum*. Flavonoids inhibited seed germination and seedling growth and caused severe necrosis and chlorosis. Based on their efficiency, flavonoids were formulated into a natural herbicide and interestingly, the extracts showed the same herbicidal effects as an industrial biopesticide containing pelargonic acid [177]. A similar study was conducted, indicating the phytotoxicity of *Plantago major* extracts on germination and seedling growth of purslane (*Portulaca oleracea*). It was observed that the level of phytotoxicity or inhibition was directly proportional to extract concentration. Phytotoxicity of a higher extract dose (40 mg mL^{-1}) was greater than the lowest one evaluated (2.5 mg mL^{-1}) and these concentrations inhibited germination by 30.24 and 4.60%, respectively. In addition, the highest concentrations significantly inhibited radical and plumule growth. The biologically active organic compounds in plant extracts were analyzed and found to be phenolics, tannins, alkaloids, flavonoids and saponins [178]. However, the compounds were not tested alone in this study, leaving no evidence of individual phytotoxic intensity of biological compounds. The need for sustainable and eco-friendly approaches in agricultural systems fosters great interest in bioproducts and biological control agents. However, further studies are required to obtain a better understanding of the many phytotoxic flavonoids.

7. Conclusions

The indispensable role of flavonoids in stress mitigation and signaling behavior in plants is highlighted. More specifically, we reviewed the protective nature of flavonoids in plants against certain biotic and abiotic stress conditions. The polyphenolic structure and diverse chemical nature of flavonoids facilitate multiple mechanisms of action, favoring plant survival under a range of harsh

conditions. Despite current knowledge of this matter, the use of flavonoids in agriculture is very limited. Soil microbiota are ecofriendly contributors in sustainable agriculture, and the iconic role of flavonoids in improving phyto-microbial associations is the "icing on the cake". Still, however, we know very little about the chemo-communications between plants and the vast number of microbial strains in the rhizosphere (phytomicrobiome members); much is left to be explored and elucidated. In addition, flavonoids play an indispensable role against plant biotic and abiotic stresses. Flavonoids could be employed as an ecofriendly and sustainable approach towards stress mitigation. The phytotoxic and pesticidal effects of flavonoids provide insight regarding how effective these biochemicals could be in the field if practically implemented. The use of bioflavonoids as natural herbicides is an area of growing interest in integrated weed management. Further research and investigations are required to understand the full range of activity of flavonoids produced naturally and/or applied artificially.

Author Contributions: Authors have contributed equally to this work. All authors have read and agreed to the published version of the manuscript.

Funding: The authors would like to acknowledge the support for this review paper was provided through the Biomass Canada Cluster (BMC), which is funded through Agriculture and Agri-Food Canada's AgriScience program and industry partners.

Acknowledgements: The authors would like to acknowledge the support for this review paper was provided through the Biomass Canada Cluster (BMC), which is funded through Agriculture and Agri-Food Canada's AgriScience program and industry partners.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Observatory Earth. World of Change: Global Temperatures. Available online: https://earthobservatory.nasa.gov/world-of-change/global-temperatures (accessed on 24 March 2020).
2. Richardson, Y.; Blin, J.; Julbe, A. A short overview on purification and conditioning of syngas produced by biomass gasification: Catalytic strategies, process intensification and new concepts. *Prog. Energy Combust. Sci.* **2012**, *38*, 765–781. [CrossRef]
3. EPA. Global Emissions by Gas. Available online: https://www.epa.gov/ghgemissions/global-greenhouse-gas-emissions-data (accessed on 24 March 2020).
4. Scialabba, N.E.-H.; Müller-Lindenlauf, M. Organic agriculture and climate change. *Renew. Agric. Food Syst.* **2010**, *25*, 158–169. [CrossRef]
5. Chalker-Scott, L. Environmental significance of anthocyanins in plant stress responses. *Photochem. Photobiol.* **1999**, *70*, 1–9. [CrossRef]
6. Chen, S.; Wu, F.; Li, Y.; Qian, Y.; Pan, X.; Li, F.; Wang, Y.; Wu, Z.; Fu, C.; Lin, H.; et al. NtMYB4 and NtCHS1 are critical factors in the regulation of flavonoid biosynthesis and are involved in salinity responsiveness. *Front. Plant Sci.* **2019**, *10*. [CrossRef] [PubMed]
7. Shojaie, B.; Mostajeran, A.; Ghanadian, M. Flavonoid dynamic responses to different drought conditions: Amount, type, and localization of flavonols in roots and shoots of *Arabidopsis thaliana* L. *Turk. J. Biol.* **2016**, *40*, 612–622. [CrossRef]
8. Brunetti, C.; Di Ferdinando, M.; Fini, A.; Pollastri, S.; Tattini, M. Flavonoids as antioxidants and developmental regulators: Relative significance in plants and humans. *Int. J. Mol. Sci.* **2013**, *14*, 3540–3555. [CrossRef] [PubMed]
9. Cushnie, T.T.; Lamb, A.J. Antimicrobial activity of flavonoids. *Int. J. Antimicrob. Agents* **2005**, *26*, 343–356. [CrossRef]
10. Singla, P.; Garg, N. Plant flavonoids: Key players in signaling, establishment, and regulation of rhizobial and mycorrhizal endosymbioses. In *Mycorrhiza-Function, Diversity, State of the Art*; Springer: Berlin/Heidelberg, Germany, 2017; pp. 133–176.
11. Liu, C.W.; Murray, J.D. The role of flavonoids in nodulation host-range specificity: An update. *Plants (Basel)* **2016**, *5*, 33. [CrossRef] [PubMed]
12. Mierziak, J.; Kostyn, K.; Kulma, A. Flavonoids as important molecules of plant interactions with the environment. *Molecules* **2014**, *19*, 16240–16265. [CrossRef]

13. Dudek, B.; Warskulat, A.-C.; Schneider, B. The Occurrence of Flavonoids and Related Compounds in Flower Sections of Papaver nudicaule. *Plants* **2016**, *5*, 28. [CrossRef]
14. Cesco, S.; Mimmo, T.; Tonon, G.; Tomasi, N.; Pinton, R.; Terzano, R.; Neumann, G.; Weisskopf, L.; Renella, G.; Landi, L.; et al. Plant-borne flavonoids released into the rhizosphere: Impact on soil bio-activities related to plant nutrition. A review. *Biol. Fertil. Soils* **2012**, *48*, 123–149. [CrossRef]
15. Nabavi, S.M.; Samec, D.; Tomczyk, M.; Milella, L.; Russo, D.; Habtemariam, S.; Suntar, I.; Rastrelli, L.; Daglia, M.; Xiao, J.; et al. Flavonoid biosynthetic pathways in plants: Versatile targets for metabolic engineering. *Biotechnol. Adv.* **2020**, *38*, 107316. [CrossRef] [PubMed]
16. Wang, Y.; Chen, S.; Yu, O. Metabolic engineering of flavonoids in plants and microorganisms. *Appl. Microbiol. Biotechnol.* **2011**, *91*, 949–956. [CrossRef] [PubMed]
17. Aherne, S.A.; O'Brien, N.M. Dietary flavonols: Chemistry, food content, and metabolism. *Nutrition* **2002**, *18*, 75–81. [CrossRef]
18. Panche, A.N.; Diwan, A.D.; Chandra, S.R. Flavonoids: An overview. *J. Nutr. Sci.* **2016**, *5*, e47. [CrossRef]
19. Samanta, A.; Das, G.; Das, S.K. Roles of Flavonoids in Plants. *Int. J. Pharm. Sci. Technol.* **2011**, *6*, 12–35.
20. Sultana, B.; Anwar, F. Flavonols (kaempeferol, quercetin, myricetin) contents of selected fruits, vegetables and medicinal plants. *Food Chem.* **2008**, *108*, 879–884. [CrossRef]
21. Crozier, A.; Lean, M.E.; McDonald, M.S.; Black, C. Quantitative analysis of the flavonoid content of commercial tomatoes, onions, lettuce, and celery. *J. Agric. Food Chem.* **1997**, *45*, 590–595. [CrossRef]
22. López-Lázaro, M. Distribution and biological activities of the flavonoid luteolin. *Mini Rev. Med. Chem.* **2009**, *9*, 31–59. [CrossRef]
23. Heim, K.E.; Tagliaferro, A.R.; Bobilya, D.J. Flavonoid antioxidants: Chemistry, metabolism and structure-activity relationships. *J. Nutr. Biochem.* **2002**, *13*, 572–584. [CrossRef]
24. Del Valle, I.; Webster, T.M.; Cheng, H.-Y.; Thies, J.E.; Kessler, A.; Miller, M.K.; Ball, Z.T.; MacKenzie, K.R.; Masiello, C.A.; Silberg, J.J.; et al. Soil organic matter attenuates the efficacy of flavonoid-based plant-microbe communication. *Sci. Adv.* **2020**, *6*, eaax8254. [CrossRef] [PubMed]
25. Erlund, I. Review of the flavonoids quercetin, hesperetin, and naringenin. Dietary sources, bioactivities, bioavailability, and epidemiology. *Nutr. Res.* **2004**, *24*, 851–874. [CrossRef]
26. Andersen, O.M.; Markham, K.R. *Flavonoids: Chemistry, Biochemistry and Applications*; CRC Press: Boca Raton, FL, USA, 2005.
27. Arts, I.C.; van de Putte, B.; Hollman, P.C. Catechin contents of foods commonly consumed in The Netherlands. 1. Fruits, vegetables, staple foods, and processed foods. *J. Agric. Food Chem.* **2000**, *48*, 1746–1751. [CrossRef] [PubMed]
28. Tsao, R. Chemistry and biochemistry of dietary polyphenols. *Nutrients* **2010**, *2*, 1231–1246. [CrossRef]
29. Hillel, D.; Hatfield, J.L. *Encyclopedia of Soils in the Environment*; Elsevier: Amsterdam, The Netherlands, 2005; Volume 3.
30. Dykhuizen, D. Species numbers in bacteria. *Proc. Calif. Acad. Sci.* **2005**, *56*, 62.
31. Lal, R.; Francaviglia, R. *Sustainable Agriculture Reviews 29: Sustainable Soil Management: Preventive and Ameliorative Strategies*; Springer: Berlin/Heidelberg, Germany, 2019; Volume 29.
32. Mia, M.B.; Shamsuddin, Z. Rhizobium as a crop enhancer and biofertilizer for increased cereal production. *Afr. J. Biotechnol.* **2010**, *9*, 6001–6009.
33. Afzal, A.; Bano, A. Rhizobium and phosphate solubilizing bacteria improve the yield and phosphorus uptake in wheat (Triticum aestivum). *Int. J. Agric. Biol.* **2008**, *10*, 85–88.
34. Hijri, M. Analysis of a large dataset of mycorrhiza inoculation field trials on potato shows highly significant increases in yield. *Mycorrhiza* **2016**, *26*, 209–214. [CrossRef]
35. Winkel-Shirley, B. Biosynthesis of flavonoids and effects of stress. *Curr. Opin. Plant Biol.* **2002**, *5*, 218–223. [CrossRef]
36. Dixon, R.A.; Pasinetti, G.M. Flavonoids and isoflavonoids: From plant biology to agriculture and neuroscience. *Plant Physiol.* **2010**, *154*, 453–457. [CrossRef]
37. Cetinkaya, H.; Kulak, M.; Karaman, M.; Karaman, H.S.; Kocer, F. Flavonoid accumulation behavior in response to the abiotic stress: Can a uniform mechanism be illustrated for all plants. In *Flavonoids—From Biosynthesis to Human Health*; Intechopen: London UK, 2017. [CrossRef]

38. Trichopoulou, A.; Vasilopoulou, E.; Hollman, P.; Chamalides, C.; Foufa, E.; Kaloudis, T.; Kromhout, D.; Miskaki, P.; Petrochilou, I.; Poulima, E.; et al. Nutritional composition and flavonoid content of edible wild greens and green pies: A potential rich source of antioxidant nutrients in the Mediterranean diet. *Food Chem.* **2000**, *70*, 319–323. [CrossRef]
39. Parvez, M.; Tomita-Yokotani, K.; Fujii, Y.; Konishi, T.; Iwashina, T. Effects of quercetin and its derivatives on the growth of Arabidopsis thaliana and Neurospora crassa. *Biochem. Syst. Ecol.* **2004**, *32*, 631–635. [CrossRef]
40. Škerget, M.; Kotnik, P.; Hadolin, M.; Hraš, A.R.; Simonič, M.; Knez, Ž. Phenols, proanthocyanidins, flavones and flavonols in some plant materials and their antioxidant activities. *Food Chem.* **2005**, *89*, 191–198. [CrossRef]
41. Díaz, M.; Rossini, C. Bioactive natural products from Sapindaceae deterrent and toxic metabolites against insects. In *Insecticides–Pest Engineering*; Perveen, F., Ed.; InTech: Rijeka, Croatia, 2012; pp. 287–308.
42. Tatsimo, S.J.N.; Tamokou, J.d.D.; Havyarimana, L.; Csupor, D.; Forgo, P.; Hohmann, J.; Kuiate, J.-R.; Tane, P. Antimicrobial and antioxidant activity of kaempferol rhamnoside derivatives from Bryophyllum pinnatum. *BMC Res. Notes* **2012**, *5*, 158. [CrossRef] [PubMed]
43. Mendki, P.; Salunke, B.; Kotkar, H.; Maheshwari, V.; Mahulikar, P.; Kothari, R. Antimicrobial and Insecticidal Activities of Flavonoid Glycosides from Calotropis procera L. for Post-harvest Preservation of Pulses. *Biopestic. Int.* **2005**, *1*, 193–200.
44. Manach, C.; Scalbert, A.; Morand, C.; Rémésy, C.; Jiménez, L. Polyphenols: Food sources and bioavailability. *Am. J. Clin. Nutr.* **2004**, *79*, 727–747. [CrossRef]
45. Wu, N.-L.; Fang, J.-Y.; Chen, M.; Wu, C.-J.; Huang, C.-C.; Hung, C.-F. Chrysin protects epidermal keratinocytes from UVA- and UVB-induced damage. *J. Agric. Food Chem.* **2011**, *59*, 8391–8400. [CrossRef]
46. Liggins, J.; Bluck, L.; Runswick, S.; Atkinson, C.; Coward, W.; Bingham, S. Daidzein and genistein contents of vegetables. *Br. J. Nutr.* **2000**, *84*, 717–725. [CrossRef]
47. Pei, Y.; Siemann, E.; Tian, B.; Ding, J. Root flavonoids are related to enhanced AMF colonization of an invasive tree. *AoB Plants* **2020**, *12*. [CrossRef]
48. Cavia-Saiz, M.; Busto, M.D.; Pilar-Izquierdo, M.C.; Ortega, N.; Perez-Mateos, M.; Muñiz, P. Antioxidant properties, radical scavenging activity and biomolecule protection capacity of flavonoid naringenin and its glycoside naringin: A comparative study. *J. Sci. Food Agric.* **2010**, *90*, 1238–1244. [CrossRef]
49. Wilmsen, P.K.; Spada, D.S.; Salvador, M. Antioxidant activity of the flavonoid hesperidin in chemical and biological systems. *J. Agric. Food Chem.* **2005**, *53*, 4757–4761. [CrossRef] [PubMed]
50. Tsai, S.M.; Phillips, D.A. Flavonoids released naturally from alfalfa promote development of symbiotic glomus spores in vitro. *Appl. Environ. Microbiol.* **1991**, *57*, 1485–1488. [CrossRef]
51. Harborne, J.B. The flavonoids: Advances in research since 1986 (Harborne, J.B.). *J. Chem. Educ.* **1995**, *72*, A73. [CrossRef]
52. Naeimi, A.F.; Alizadeh, M. Antioxidant properties of the flavonoid fisetin: An updated review of in vivo and in vitro studies. *Trends Food Sci. Technol.* **2017**, *70*, 34–44. [CrossRef]
53. Ong, K.C.; Khoo, H.-E. Biological effects of myricetin. *Gen. Pharmacol. Vasc. Syst.* **1997**, *29*, 121–126. [CrossRef]
54. Peters, N.; Frost, J.; Long, S. A plant flavone, luteolin, induces expression of Rhizobium meliloti nodulation genes. *Science* **1986**, *233*, 977–980. [CrossRef]
55. Garcia, K.; Delaux, P.M.; Cope, K.R.; Ane, J.M. Molecular signals required for the establishment and maintenance of ectomycorrhizal symbioses. *New Phytol.* **2015**, *208*, 79–87. [CrossRef]
56. Rice-evans, C.A.; Miller, N.J.; Bolwell, P.G.; Bramley, P.M.; Pridham, J.B. The relative antioxidant activities of plant-derived polyphenolic flavonoids. *Free Radic. Res.* **1995**, *22*, 375–383. [CrossRef]
57. Tsanova-Savova, S.; Ribarova, F.; Gerova, M. (+)-Catechin and (−)-epicatechin in Bulgarian fruits. *J. Food Compos. Anal.* **2005**, *18*, 691–698. [CrossRef]
58. Pathan, S.I.; Ceccherini, M.T.; Sunseri, F.; Lupini, A. Rhizosphere as hotspot for plant-soil-microbe interaction. In *Carbon and Nitrogen Cycling in Soil*; Springer: Berlin/Heidelberg, Germany, 2020; pp. 17–43.
59. Mandal, S.M.; Chakraborty, D.; Dey, S. Phenolic acids act as signaling molecules in plant-microbe symbioses. *Plant Signal. Behav.* **2010**, *5*, 359–368. [CrossRef]

60. Sugiyama, A.; Shitan, N.; Yazaki, K. Involvement of a soybean ATP-binding cassette-type transporter in the secretion of genistein, a signal flavonoid in legume-Rhizobium symbiosis. *Plant Physiol.* **2007**, *144*, 2000–2008. [CrossRef]
61. Shaw, L.J.; Morris, P.; Hooker, J.E. Perception and modification of plant flavonoid signals by rhizosphere microorganisms. *Environ. Microbiol.* **2006**, *8*, 1867–1880. [CrossRef] [PubMed]
62. Kovács, E.; Keresztes, Á. Effect of gamma and UV-B/C radiation on plant cells. *Micron* **2002**, *33*, 199–210. [CrossRef]
63. Chaparro, J.M.; Sheflin, A.M.; Manter, D.K.; Vivanco, J.M. Manipulating the soil microbiome to increase soil health and plant fertility. *Biol. Fertil. Soils* **2012**, *48*, 489–499. [CrossRef]
64. Munoz Aguilar, J.M.; Ashby, A.M.; Richards, A.J.M.; Loake, G.J.; Watson, M.D.; Shaw, C.H. Chemotaxis of Rhizobium leguminosarum biovar phaseoli towards flavonoid inducers of the symbiotic nodulation genes. *Microbiology* **1988**, *134*, 2741–2746. [CrossRef]
65. Hassan, S.; Mathesius, U. The role of flavonoids in root-rhizosphere signalling: Opportunities and challenges for improving plant-microbe interactions. *J. Exp. Bot.* **2012**, *63*, 3429–3444. [CrossRef]
66. Bolaños-Vásquez, M.C.; Werner, D. Effects of Rhizobium tropici, R. etli, and R. leguminosarum bv. phaseoli on nod gene-inducing flavonoids in root exudates of Phaseolus vulgaris. *Mol. Plant Microbe Interact.* **1997**, *10*, 339–346. [CrossRef]
67. Stambulska, U.Y.; Bayliak, M.M. Legume-rhizobium symbiosis: Secondary metabolites, free radical processes, and effects of heavy metals. In *Bioactive Molecules in Food*; Springer: Berlin/Heidelberg, Germany, 2019; pp. 1–32. [CrossRef]
68. Davidson, E.A. The contribution of manure and fertilizer nitrogen to atmospheric nitrous oxide since 1860. *Nat. Geosci.* **2009**, *2*, 659–662. [CrossRef]
69. Hartwig, U.A.; Joseph, C.M.; Phillips, D.A. Flavonoids released naturally from alfalfa seeds enhance growth rate of Rhizobium meliloti. *Plant Physiol.* **1991**, *95*, 797–803. [CrossRef]
70. Maxwell, C.A.; Hartwig, U.A.; Joseph, C.M.; Phillips, D.A. A chalcone and two related flavonoids released from alfalfa roots induce *nod* genes of *Rhizobium meliloti*. *Plant Physiol.* **1989**, *91*, 842–847. [CrossRef]
71. Dolatabadian, A.; Sanavy, S.A.M.M.; Ghanati, F.; Gresshoff, P.M. Morphological and physiological response of soybean treated with the microsymbiont Bradyrhizobium japonicum pre-incubated with genistein. *S. Afr. J. Bot.* **2012**, *79*, 9–18. [CrossRef]
72. Subramanian, S.; Stacey, G.; Yu, O. Endogenous isoflavones are essential for the establishment of symbiosis between soybean and Bradyrhizobium japonicum. *Plant J.* **2006**, *48*, 261–273. [CrossRef] [PubMed]
73. Jones, F.R.; Tisdale, W. Effect of soil temperature upon the development of nodules on the roots of certain legumes. *J. Agric. Res.* **1921**, *22*, 17–37.
74. Lynch, D.; Smith, D. Soybean (Glycine max) modulation and N2-fixation as affected by exposure to a low root-zone temperature. *Physiol. Plant.* **1993**, *88*, 212–220. [CrossRef]
75. Pan, B.; Zhang, F.; Smith, D.L. Genistein addition to the rooting medium of soybean at the onset of nitrogen fixation increases nodulation. *J. Plant Nutr.* **1998**, *21*, 1631–1639. [CrossRef]
76. Gibson, A. Factors in the physical and biological environment affecting nodulation and nitrogen fixation by legumes. *Plant Soil* **1971**, *35*, 139–152. [CrossRef]
77. Layzell, D.; Rochman, P.; Canvin, D. Low root temperatures and nitrogenase activity in soybean. *Can. J. Bot.* **1984**, *62*, 965–971. [CrossRef]
78. Zhang, F.; Smith, D.L. Preincubation of bradyrhizobium japonicum with genistein accelerates nodule development of soybean at suboptimal root zone temperatures. *Plant Physiol.* **1995**, *108*, 961–968. [CrossRef]
79. Kasper, S.; Christoffersen, B.; Soti, P.; Racelis, A. Abiotic and biotic limitations to nodulation by leguminous cover crops in South Texas. *Agriculture* **2019**, *9*, 209. [CrossRef]
80. Hemida, M.; Issa, A.A.; Ohyam, T. Impact of harsh environmental conditions on nodule formation and dinitrogen fixation of legumes. In *Advances in Biology and Ecology of Nitrogen Fixation*; Intechopen: London, UK, 2014. [CrossRef]
81. Zhang, F.; Smith, D.L. Application of genistein to inocula and soil to overcome low spring soil temperature inhibition of soybean nodulation and nitrogen fixation. *Plant Soil* **1997**, *192*, 141–151. [CrossRef]

82. Belkheir, A.M.; Zhou, X.; Smith, D.L. Variability in yield and yield component responses to genistein pre-incubated Bradyrhizobium japonicum by soybean [Glycine max (L.) Merr] cultivars. *Plant soil* **2001**, *229*, 41–46. [CrossRef]
83. Belkheir, A.; Zhou, X.; Smith, D. Response of soybean [Glycine max (L.) Merr.] cultivars to genistein-preincubated bradyrhizobium japonicum: Nodulation and dry matter accumulation under Canadian short-season conditions. *J. Agron. Crop Sci.* **2000**, *185*, 167–175. [CrossRef]
84. Morrison, M.; Cober, E.; Saleem, M.; McLaughlin, N.; Fregeau-Reid, J.; Ma, B.; Yan, W.; Woodrow, L. Changes in isoflavone concentration with 58 years of genetic improvement of short-season soybean cultivars in Canada. *Crop Sci.* **2008**, *48*, 2201–2208. [CrossRef]
85. Hinsinger, P. Bioavailability of soil inorganic P in the rhizosphere as affected by root-induced chemical changes: A review. *Plant soil* **2001**, *237*, 173–195. [CrossRef]
86. Mohammadi, K.; Khalesro, S.; Sohrabi, Y.; Heidari, G. A review: Beneficial effects of the mycorrhizal fungi for plant growth. *J. Appl. Environ. Biol. Sci.* **2011**, *1*, 310–319.
87. Parniske, M. Arbuscular mycorrhiza: The mother of plant root endosymbioses. *Nat. Rev. Microbiol.* **2008**, *6*, 763–775. [CrossRef]
88. Vierheilig, H.; Bago, B.; Albrecht, C.; Poulin, M.-J.; Piché, Y. Flavonoids and arbuscular-mycorrhizal fungi. In *Flavonoids in the Living System*; Manthey, J.A., Buslig, B.S., Eds.; Springer: Boston, MA, USA, 1998; pp. 9–33. [CrossRef]
89. Becard, G.; Taylor, L.P.; Douds, D.D.; Pfeffer, P.E.; Doner, L.W. Flavonoids are not necessary plant signal compounds in arbuscular mycorrhizal symbioses. *MPMI Mol. Plant Microbe Interact.* **1995**, *8*, 252–258. [CrossRef]
90. Siqueira, J.; Safir, G.; Nair, M. Stimulation of vesicular-arbuscular mycorrhiza formation and growth of white clover by flavonoid compounds. *New Phytol.* **1991**, *118*, 87–93. [CrossRef]
91. Davies, F.T.; Calderón, C.M.; Huaman, Z. Influence of arbuscular mycorrhizae indigenous to peru and a flavonoid on growth, yield, and leaf elemental concentration of 'yungay'potatoes. *HortScience* **2005**, *40*, 381–385. [CrossRef]
92. Davies, F.T., Jr.; Calderón, C.M.; Huaman, Z.; Gómez, R. Influence of a flavonoid (formononetin) on mycorrhizal activity and potato crop productivity in the highlands of Peru. *Sci. Hortic.* **2005**, *106*, 318–329. [CrossRef]
93. De Almeida Ribeiro, P.R.; dos SANTOS, J.V.; de Carvalho, T.S.; da Silva, J.S.; de Resende, P.M.; de Souza Moreira, F.M. Formononetin associated with phosphorus influences soybean symbiosis with mycorrhizal fungi and Bradyrhizobium. *Biosci. J.* **2016**, *32*.
94. Scervino, J.M.; Ponce, M.A.; Erra-Bassells, R.; Bompadre, J.; Vierheilig, H.; Ocampo, J.A.; Godeas, A. The effect of flavones and flavonols on colonization of tomato plants by arbuscular mycorrhizal fungi of the genera Gigaspora and Glomus. *Can. J. microbiol.* **2007**, *53*, 702–709. [CrossRef] [PubMed]
95. Nakabayashi, R.; Mori, T.; Saito, K. Alternation of flavonoid accumulation under drought stress in Arabidopsis thaliana. *Plant Signal. Behav.* **2014**, *9*, e29518. [CrossRef]
96. Dakora, F.D.; Phillips, D.A. Root exudates as mediators of mineral acquisition in low-nutrient environments. *Plant Soil* **2002**, *245*, 35–47. [CrossRef]
97. Gupta, R.; Chakrabarty, S. Gibberellic acid in plant: Still a mystery unresolved. *Plant Signal. Behav.* **2013**, *8*, e25504. [CrossRef]
98. Tomasi, N.; Weisskopf, L.; Renella, G.; Landi, L.; Pinton, R.; Varanini, Z.; Nannipieri, P.; Torrent, J.; Martinoia, E.; Cesco, S. Flavonoids of white lupin roots participate in phosphorus mobilization from soil. *Soil Biol. Biochem.* **2008**, *40*, 1971–1974. [CrossRef]
99. Cesco, S.; Neumann, G.; Tomasi, N.; Pinton, R.; Weisskopf, L. Release of plant-borne flavonoids into the rhizosphere and their role in plant nutrition. *Plant Soil* **2010**, *329*, 1–25. [CrossRef]
100. Cramer, G.R.; Urano, K.; Delrot, S.; Pezzotti, M.; Shinozaki, K. Effects of abiotic stress on plants: A systems biology perspective. *BMC Plant Biol.* **2011**, *11*, 163. [CrossRef]
101. Haak, D.C.; Fukao, T.; Grene, R.; Hua, Z.; Ivanov, R.; Perrella, G.; Li, S. Multilevel regulation of abiotic stress responses in plants. *Front. Plant Sci.* **2017**, *8*, 1564. [CrossRef]

102. Nihorimbere, V.; Ongena, M.; Smargiassi, M.; Thonart, P. Beneficial effect of the rhizosphere microbial community for plant growth and health. *Biotechnol. Agron. Soc. Environ.* **2011**, *15*, 327–337.
103. Walker, T.S.; Bais, H.P.; Grotewold, E.; Vivanco, J.M. Root exudation and rhizosphere biology. *Plant Physiol.* **2003**, *132*, 44–51. [CrossRef] [PubMed]
104. Chen, H.; Gao, H.; Fang, X.; Ye, L.; Zhou, Y.; Yang, H. Effects of allyl isothiocyanate treatment on postharvest quality and the activities of antioxidant enzymes of mulberry fruit. *Postharvest Biol. Technol.* **2015**, *108*, 61–67. [CrossRef]
105. Solovchenko, A.; Schmitz-Eiberger, M. Significance of skin flavonoids for UV-B-protection in apple fruits. *J. Exp. Bot.* **2003**, *54*, 1977–1984. [CrossRef] [PubMed]
106. Mariz-Ponte, N.; Mendes, R.; Sario, S.; de Oliveira, J.F.; Melo, P.; Santos, C. Tomato plants use non-enzymatic antioxidant pathways to cope with moderate UV-A/B irradiation: A contribution to the use of UV-A/B in horticulture. *J. Plant Physiol.* **2018**, *221*, 32–42. [CrossRef]
107. Merzlyak, M.N.; Solovchenko, A.E.; Gitelson, A.A. Reflectance spectral features and non-destructive estimation of chlorophyll, carotenoid and anthocyanin content in apple fruit. *Postharvest Biol. Technol.* **2003**, *27*, 197–211. [CrossRef]
108. Schmitz-Hoerner, R.; Weissenböck, G. Contribution of phenolic compounds to the UV-B screening capacity of developing barley primary leaves in relation to DNA damage and repair under elevated UV-B levels. *Phytochemistry* **2003**, *64*, 243–255. [CrossRef]
109. Tossi, V.; Lombardo, C.; Cassia, R.; Lamattina, L. RETRACTED: Nitric oxide and flavonoids are systemically induced by UV-B in maize leaves. *Plant Sci.* **2012**, *193–194*, 103–109. [CrossRef]
110. Pathan, M.S.; Lee, J.-D.; Shannon, J.G.; Nguyen, H.T. Recent advances in breeding for drought and salt stress tolerance in soybean. In *Advances in Molecular Breeding Toward Drought and Salt Tolerant Crops*; Jenks, M.A., Hasegawa, P.M., Jain, S.M., Eds.; Springer: Dordrecht, The Netherlands, 2007; pp. 739–773. [CrossRef]
111. Ilangumaran, G.; Smith, D.L. Plant growth promoting rhizobacteria in amelioration of salinity stress: A systems biology perspective. *Front. Plant Sci.* **2017**, *8*, 1768. [CrossRef]
112. Greenway, H.; Munns, R. Mechanisms of salt tolerance in nonhalophytes. *Ann. Rev. Plant Physiol.* **1980**, *31*, 149–190. [CrossRef]
113. Chaves, M.M.; Flexas, J.; Pinheiro, C. Photosynthesis under drought and salt stress: Regulation mechanisms from whole plant to cell. *Ann. Bot.* **2009**, *103*, 551–560. [CrossRef]
114. Perri, S.; Entekhabi, D.; Molini, A. Plant osmoregulation as an emergent water-saving adaptation. *Water Resour. Res.* **2018**, *54*, 2781–2798. [CrossRef]
115. Bernstein, N. Plants and salt: Plant response and adaptations to salinity. In *Model Ecosystems in Extreme Environments*; Elsevier: Amsterdam, The Netherlands, 2019; pp. 101–112.
116. Jones, G.W.; Gorham, J. Intra-and Inter-Cellular Compartmentation of Ions. In *Salinity: Environment-Plants-Molecules*; Springer: Dordrecht, The Netherlands, 2002; pp. 159–180.
117. Flowers, T.J.; Colmer, T.D. Salinity tolerance in halophytes. *New Phytol.* **2008**, *179*, 945–963. [CrossRef] [PubMed]
118. Munns, R.; Tester, M. Mechanisms of salinity tolerance. *Ann. Rev. Plant Biol.* **2008**, *59*, 651–681. [CrossRef] [PubMed]
119. Koyro, H.-W. Effect of salinity on growth, photosynthesis, water relations and solute composition of the potential cash crop halophyte *Plantago coronopus* (L.). *Environ. Exp. Bot.* **2006**, *56*, 136–146. [CrossRef]
120. Rhodes, D.; Nadolska-Orczyk, A.; Rich, P. Salinity, osmolytes and compatible solutes. In *Salinity: Environment-Plants-Molecules*; Springer: Dordrecht, The Netherlands, 2002; pp. 181–204.
121. Al Hassan, M.; MartÍNez Fuertes, M.; Ramos SÁNchez, F.J.; Vicente, O.; Boscaiu, M. Effects of salt and water stress on plant growth and on accumulation of osmolytes and antioxidant compounds in cherry tomato. *Not. Bot. Horti Agrobot. Cluj Napoca* **2015**, *43*, 1–11. [CrossRef]
122. AbdElgawad, H.; Zinta, G.; Hegab, M.M.; Pandey, R.; Asard, H.; Abuelsoud, W. High salinity induces different oxidative stress and antioxidant responses in maize seedlings organs. *Front. Plant Sci.* **2016**, *7*, 276. [CrossRef]
123. Wang, H.-M.; Xiao, X.-R.; Yang, M.-Y.; Gao, Z.-L.; Zang, J.; Fu, X.-M.; Chen, Y.-H. Effects of salt stress on antioxidant defense system in the root of Kandelia candel. *Bot. Stud.* **2014**, *55*, 57. [CrossRef]
124. Abogadallah, G.M. Antioxidative defense under salt stress. *Plant Signal. Behav.* **2010**, *5*, 369–374. [CrossRef]

125. Engwa, G.A. Free radicals and the role of plant phytochemicals as antioxidants against oxidative stress-related diseases. In *Phytochemicals: Source of Antioxidants and Role in Disease Prevention. BoD–Books on Demand*; Intechopen: London, UK, 2018; pp. 49–74.
126. Halliwell, B.; Gutteridge, J.M.C. *Free Radicals in Biology and Medicine*, 5th ed.; Oxford University Press: New York, NY, USA, 2015.
127. Smith, A.M.; Ratcliffe, R.G.; Sweetlove, L.J. Activation and function of mitochondrial uncoupling protein in plants. *J. Biol. Chem.* **2004**, *279*, 51944–51952. [CrossRef]
128. Pietta, P.-G. Flavonoids as antioxidants. *J. Nat. Prod.* **2000**, *63*, 1035–1042. [CrossRef]
129. Lü, J.M.; Lin, P.H.; Yao, Q.; Chen, C. Chemical and molecular mechanisms of antioxidants: Experimental approaches and model systems. *J. Cell. Mol. Med.* **2010**, *14*, 840–860. [CrossRef] [PubMed]
130. Di Ferdinando, M.; Brunetti, C.; Fini, A.; Tattini, M. Flavonoids as antioxidants in plants under abiotic stresses. In *Abiotic Stress Responses in Plants*; Springer: New York, NY, USA, 2012; pp. 159–179. [CrossRef]
131. Kaliamoortiiy, S.; Rao, A. Effect of salinity on anthocyanin accumulation in the root of maize. *Science* **1994**, *248*, 1637–1638.
132. Sugiyama, A.; Yazaki, K. Flavonoids in plant rhizospheres: Secretion, fate and their effects on biological communication. *Plant Biotechnol.* **2014**, *31*, 431–443. [CrossRef]
133. Miransari, M.; Smith, D. Overcoming the stressful effects of salinity and acidity on soybean nodulation and yields using signal molecule genistein under field conditions. *J. Plant Nutr.* **2007**, *30*, 1967–1992. [CrossRef]
134. Miransari, M.; Smith, D. Alleviating salt stress on soybean (Glycine max (L.) Merr.)–Bradyrhizobium japonicum symbiosis, using signal molecule genistein. *Eur. J. Soil Biol.* **2009**, *45*, 146–152. [CrossRef]
135. Ma, D.; Sun, D.; Wang, C.; Li, Y.; Guo, T. Expression of flavonoid biosynthesis genes and accumulation of flavonoid in wheat leaves in response to drought stress. *Plant Physiol. Biochem.* **2014**, *80*, 60–66. [CrossRef]
136. Varela, M.C.; Arslan, I.; Reginato, M.A.; Cenzano, A.M.; Luna, M.V. Phenolic compounds as indicators of drought resistance in shrubs from Patagonian shrublands (Argentina). *Plant Physiol. Biochem.* **2016**, *104*, 81–91. [CrossRef]
137. Koes, R.E.; Quattrocchio, F.; Mol, J.N. The flavonoid biosynthetic pathway in plants: Function and evolution. *BioEssays* **1994**, *16*, 123–132. [CrossRef]
138. Maddox, C.E.; Laur, L.M.; Tian, L. Antibacterial activity of phenolic compounds against the phytopathogen Xylella fastidiosa. *Curr. Microbiol.* **2010**, *60*, 53. [CrossRef]
139. Rattan, R.S. Mechanism of action of insecticidal secondary metabolites of plant origin. *Crop Prot.* **2010**, *29*, 913–920. [CrossRef]
140. Kaplan, D.; Keen, N.; Thomason, I. Studies on the mode of action of glyceollin in soybean incompatibility to the root knot nematode, Meloidogyne incognita. *Physiol. Plant Pathol.* **1980**, *16*, 319–325. [CrossRef]
141. Chin, S.; Behm, C.A.; Mathesius, U. Functions of flavonoids in plant(-)nematode interactions. *Plants (Basel)* **2018**, *7*, 85. [CrossRef] [PubMed]
142. Huang, J.-S.; Barker, K.R. Glyceollin I in soybean-cyst nematode interactions: Spatial and temporal distribution in roots of resistant and susceptible soybeans. *Plant Physiol.* **1991**, *96*, 1302–1307. [CrossRef] [PubMed]
143. Soriano, I.; Asenstorfer, R.; Schmidt, O.; Riley, I. Inducible flavone in oats (Avena sativa) is a novel defense against plant-parasitic nematodes. *Phytopathology* **2004**, *94*, 1207–1214. [CrossRef] [PubMed]
144. Fawe, A.; Abou-Zaid, M.; Menzies, J.; Bélanger, R. Silicon-mediated accumulation of flavonoid phytoalexins in cucumber. *Phytopathology* **1998**, *88*, 396–401. [CrossRef]
145. del Río, J.A.; Gómez, P.; Baidez, A.G.; Arcas, M.C.; Botía, J.M.; Ortuño, A. Changes in the levels of polymethoxyflavones and flavanones as part of the defense mechanism of citrus sinensis (Cv. Valencia Late) fruits against phytophthora citrophthora. *J. Agric. Food Chem.* **2004**, *52*, 1913–1917. [CrossRef]
146. Ortuno, A.; Arcas, M.; Botia, J.; Fuster, M.; Del Río, J. Increasing resistance against Phytophthora citrophthora in tangelo Nova fruits by modulating polymethoxyflavones levels. *J. Agric. Food Chem.* **2002**, *50*, 2836–2839. [CrossRef]
147. Boué, S.M.; Carter, C.H.; Ehrlich, K.C.; Cleveland, T.E. Induction of the soybean phytoalexins coumestrol and glyceollin by Aspergillus. *J. Agric. Food Chem.* **2000**, *48*, 2167–2172. [CrossRef]
148. Cushnie, T.P.; Lamb, A.J. Recent advances in understanding the antibacterial properties of flavonoids. *Int. J. Antimicrob. Agents* **2011**, *38*, 99–107. [CrossRef]

149. Gnanamanickam, S.S.; Patil, S.S. Accumulation of antibacterial isoflavonoids in hypersensitively responding bean leaf tissues inoculated with Pseudomonas phaseolicola. *Physiol. Plant Pathol.* **1977**, *10*, 159–168. [CrossRef]
150. Lyon, F.M.; Wood, R. Production of phaseollin, coumestrol and related compounds in bean leaves inoculated with Pseudomonas spp. *Physiol. Plant Pathol.* **1975**, *6*, 117–124. [CrossRef]
151. Keen, N.; Kennedy, B. Hydroxyphaseollin and related isoflavanoids in the hypersensitive resistance reaction of soybeans to Pseudomonas glycinea. *Physiol. Plant Pathol.* **1974**, *4*, 173–185. [CrossRef]
152. Wyman, J.G. Antibacterial activity of selected isoflavonoids. *Phytopathology* **1978**, *68*, 583. [CrossRef]
153. Tanaka, H.; Sato, M.; Oh-Uchi, T.; Yamaguchi, R.; Etoh, H.; Shimizu, H.; Sako, M.; Takeuchi, H. Antibacterial properties of a new isoflavonoid from Erythrina poeppigiana against methicillin-resistant Staphylococcus aureus. *Phytomedicine* **2004**, *11*, 331–337. [CrossRef] [PubMed]
154. War, A.R.; Paulraj, M.G.; Ahmad, T.; Buhroo, A.A.; Hussain, B.; Ignacimuthu, S.; Sharma, H.C. Mechanisms of plant defense against insect herbivores. *Plant Signal. Behav.* **2012**, *7*, 1306–1320. [CrossRef] [PubMed]
155. Gao, Q.-M.; Zhu, S.; Kachroo, P.; Kachroo, A. Signal regulators of systemic acquired resistance. *Front. Plant Sci.* **2015**, *6*. [CrossRef]
156. Tridiptasari, A.; Brawijaya, U.; Leksono, A.S.; Siswanto, D. Antifeedant Effect of *Moringa oleifera* (L.) Leaf and Seed Extract on Growth and Feeding Activity of Spodoptera litura (Fab.) (Lepidoptera: Noctuidae). *J. Exp. Life Sci.* **2019**, *9*, 25–31. [CrossRef]
157. Aljbory, Z.; Chen, M.S. Indirect plant defense against insect herbivores: A review. *Insect Sci.* **2018**, *25*, 2–23. [CrossRef]
158. Rosell, G.; Quero, C.; Coll, J.; Guerrero, A. Biorational insecticides in pest management. *J. Pestic. Sci.* **2008**, *33*, 103–121. [CrossRef]
159. Quiroz, A.; Mendez, L.; Mutis, A.; Hormazabal, E.; Ortega, F.; Birkett, M.A.; Parra, L. Antifeedant activity of red clover root isoflavonoids on Hylastinus obscurus. *J. Soil Sci. Plant Nutr.* **2017**, *17*, 231–239. [CrossRef]
160. Goławska, S.; Lukasik, I. Antifeedant activity of luteolin and genistein against the pea aphid, Acyrthosiphon pisum. *J. Pest. Sci. (2004)* **2012**, *85*, 443–450. [CrossRef] [PubMed]
161. Johnson, E.T.; Dowd, P.F. Differentially enhanced insect resistance, at a cost, in Arabidopsis thaliana constitutively expressing a transcription factor of defensive metabolites. *J. Agric. Food Chem.* **2004**, *52*, 5135–5138. [CrossRef] [PubMed]
162. Simmonds, M.S. Importance of flavonoids in insect–plant interactions: Feeding and oviposition. *Phytochemistry* **2001**, *56*, 245–252. [CrossRef]
163. Lattanzio, V.; Lattanzio, V.M.; Cardinali, A. Role of phenolics in the resistance mechanisms of plants against fungal pathogens and insects. *Phytochem. Adv. Res.* **2006**, *661*, 23–67.
164. Nenaah, G.E. Toxic and antifeedant activities of prenylated flavonoids isolated from Tephrosia apollinea L. against three major coleopteran pests of stored grains with reference to their structure–activity relationship. *Nat. Prod. Res.* **2014**, *28*, 2245–2252. [CrossRef]
165. Weston, L.A.; Duke, S.O. Weed and crop allelopathy. *Crit. Rev. Plant Sci.* **2003**, *22*, 367–389. [CrossRef]
166. Oerke, E.C. Crop losses to pests. *J. Agric. Sci.* **2005**, *144*, 31–43. [CrossRef]
167. Young, S.L.; Pierce, F.J. *Automation: The Future of Weed Control*; Springer Science and Business Media: Berlin/Heidelberg, Germany, 2013.
168. Molisch, H. *Der Einfluss Einer Pflanze Auf die Andere, Allelopathie*; Fischer: Jena, Germany, 1937.
169. Rice, E. *Allelopathy*, 2nd ed.; Acad. Press Inc.: Orlando, FL, USA, 1984; p. 422.
170. Rob, M.M.; Hossen, K.; Iwasaki, A.; Suenaga, K.; Kato-Noguchi, H. Phytotoxic activity and identification of phytotoxic substances from schumannianthus dichotomus. *Plants* **2020**, *9*, 102. [CrossRef]
171. Jabran, K.; Mahajan, G.; Sardana, V.; Chauhan, B.S. Allelopathy for weed control in agricultural systems. *Crop Prot.* **2015**, *72*, 57–65. [CrossRef]
172. Alsaadawi, I.S.; Sarbout, A.K.; Al-Shamma, L.M. Differential allelopathic potential of sunflower (*Helianthus annuus* L.) genotypes on weeds and wheat (*Triticum aestivum* L.) crop. *Arch. Agron. Soil Sci.* **2012**, *58*, 1139–1148. [CrossRef]
173. Palma-Tenango, M.; Soto-Hernández, M.; Aguirre-Hernández, E. Flavonoids in agriculture. In *Flavonoids—From Biosynthesis to Human Health*; Intech: Rijeka, Croatia, 2017. [CrossRef]
174. Weston, L.A.; Mathesius, U. Flavonoids: Their structure, biosynthesis and role in the rhizosphere, including allelopathy. *J. Chem. Ecol.* **2013**, *39*, 283–297. [CrossRef] [PubMed]

175. Zhang, H.; Gao, J.-M.; Liu, W.-T.; Tang, J.-C.; Zhang, X.-C.; Jin, Z.-G.; Xu, Y.-P.; Shao, M.-A. Allelopathic substances from walnut (Juglans regia L.) leaves. *Allelopath. J.* **2008**, *21*, 425–431.
176. Yan, Z.; Guo, H.; Yang, J.; Liu, Q.; Jin, H.; Xu, R.; Cui, H.; Qin, B. Phytotoxic flavonoids from roots of Stellera chamaejasme L. (Thymelaeaceae). *Phytochemistry* **2014**, *106*, 61–68. [CrossRef] [PubMed]
177. Kaab, S.B.; Rebey, I.B.; Hanafi, M.; Hammi, K.M.; Smaoui, A.; Fauconnier, M.L.; De Clerck, C.; Jijakli, M.H.; Ksouri, R. Screening of Tunisian plant extracts for herbicidal activity and formulation of a bioherbicide based on Cynara cardunculus. *S. Afr. J. Bot.* **2020**, *128*, 67–76. [CrossRef]
178. Al-obaidi, A.F. Phytotoxicity of plantago major extracts on germination and seedling growth of purslane (portulaca oleracea). In *Seed Dormancy and Germination*; IntechOpen: London, UK, 2020.