



Review

# Carbon Fluxes between Primary Metabolism and Phenolic Pathway in Plant Tissues under Stress

Sofia Caretto <sup>1</sup>, Vito Linsalata <sup>2</sup>, Giovanni Colella <sup>1</sup>, Giovanni Mita <sup>1</sup> and Vincenzo Lattanzio <sup>3,\*</sup>

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<sup>1</sup> Institute of Sciences of Food Production, National Research Council, Via Provinciale Lecce-Monteroni, 73100 Lecce, Italy; sofia.caretto@ispa.cnr.it (S.C.); gianni.colella@ispa.cnr.it (G.C.); giovanni.mita@ispa.cnr.it (G.M.)

<sup>2</sup> Institute of Sciences of Food Production, National Research Council, Via Amendola, 122/O, 70126 Bari, Italy; vito.linsalata@ispa.cnr.it

<sup>3</sup> Department of Sciences of Agriculture, Food and Environment, University of Foggia, Via Napoli 25, 71100 Foggia, Italy

\* Correspondence: vincenzo.lattanzio@unifg.it; Tel.: +39-320-4394738

**Abstract:** Higher plants synthesize an amazing diversity of phenolic secondary metabolites. Phenolics are defined secondary metabolites or natural products because, originally, they were considered not essential for plant growth and development. Plant phenolics, like other natural compounds, provide the plant with specific adaptations to changing environmental conditions and, therefore, they are essential for plant defense mechanisms. Plant defensive traits are costly for plants due to the energy drain from growth toward defensive metabolite production. Being limited with environmental resources, plants have to decide how allocate these resources to various competing functions. This decision brings about trade-offs, *i.e.*, promoting some functions by neglecting others as an inverse relationship. Many studies have been carried out in order to link an evaluation of plant performance (in terms of growth rate) with levels of defense-related metabolites. Available results suggest that environmental stresses and stress-induced phenolics could be linked by a transduction pathway that involves: (i) the proline redox cycle; (ii) the stimulated oxidative pentose phosphate pathway; and, in turn, (iii) the reduced growth of plant tissues.

**Keywords:** environmental stresses; phenolics; resistance costs; trade-offs; proline; transduction pathway

## 1. Plant Phenolic Secondary Metabolites

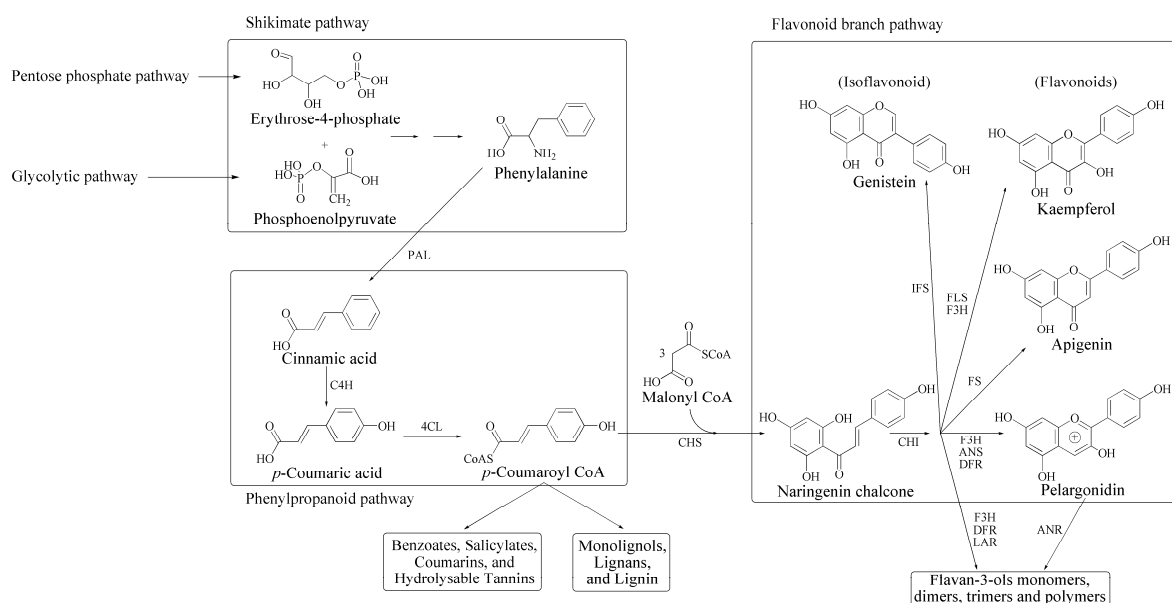
Higher plants produce a bewildering number of chemical compounds (more than 200,000 different structures). These compounds can be classified as belonging to primary or secondary metabolites, also called natural products. Primary metabolites are ubiquitous in plants and fulfill essential metabolic roles. Natural products refer to compounds that are differentially distributed in the plant kingdom and fulfill a very broad range of physiological roles that are considered essential for their adaptive significance in protection against environmental constraints. Nowadays, it is widely recognized that natural products play a role in plant growth, reproduction, and the continued survival of land plants [1–3].

Plants exhibit a variable qualitative and quantitative distribution of natural products in different tissues and organs. This variability is also observed between different physiological stages, between individuals, and between populations [4–8]. Plants synthesize amounts of natural products under genetic control upon environmental stimuli. These natural products are synthesized in plants through metabolic pathways, which are an integral part of the whole plant developmental program,

as a response to stress conditions induced by biotic and abiotic agents. A strict genetic and epigenetic control of these pathways guarantees the proper production profile of different secondary metabolites. Their transport represents an additional level of regulation [9–15].

Plant phenolics are the most widely distributed natural products. In leaf extracts of vascular plants several classes of phenolic compounds such as esters, amides, and glycosides of hydroxycinnamic acids, flavonoids, proanthocyanidins, and their relatives can be found. In addition, polymeric phenolics, such as lignin, suberin, and melanins, can be commonly found in these plants [16–19]. (Poly)phenolic compounds are produced in plants by the sequential action of five biosynthetic pathways. The glycolytic and pentose phosphate pathways provide precursors (phosphoenolpyruvate and erythrose-4-phosphate, respectively) to the shikimate pathway. Phenylalanine, produced by the shikimate route, is the precursor of phenylpropanoid metabolism which, in turn, feeds the diverse specific flavonoid pathways (Figure 1) [20–26].

Phenolic compounds have been produced in plants because of the interactions with the challenging environment throughout the course of evolution. This production has been an event of paramount importance for the colonization of land. In this connection, plant phenolics represent a noticeable example of plant metabolic plasticity that enable plants to survive environmental stresses. Indeed, when the first plants moved from water to land, they were forced to cope with stressful conditions, such as ultraviolet (UV) radiation [8,27–29]. At that time, the ability of UV radiation to severely damage biomolecules induced land plants to synthesize phenolic molecules (starting from the shikimate pathway, Figure 1) to be used as sunscreens, about 480–360 million years ago. In algae, the shikimate pathway only produces phenylalanine and tyrosine, which are already present in proteins of primordial bacteria. Aerobic bacteria and algae produce polyketides through the condensation of acetyl-CoA as a starter unit and malonyl-CoA for chain elongation. In bryophytes, the starter unit acetyl-CoA was substituted by cinnamoyl-CoA, leading to flavones and flavonols, which, absorbing UV light, act as photoscreens in all terrestrial plants [30–32].



**Figure 1.** General biosynthetic pathway of phenylpropanoid and flavonoid structures. PAL, phenylalanine ammonia-lyase; C4H, cinnamate-4-hydroxylase; 4CL, 4-coumaroyl:CoA-ligase; CHS, chalcone synthase; CHI, chalcone isomerase; ANS, anthocyanidin synthase; DFR, dihydroflavonol reductase; FS, flavone synthase; FLS, flavonol synthase; F3H, flavanone 3-hydroxylase; IFS, isoflavone synthase; ANR, anthocyanidin reductase; LAR, leucoanthocyanidin reductase (redrawn from [26] with permission of Elsevier).

Besides UV radiation, other stress factors are present in an aerial environment which require the adaptation of plant metabolism. Once more, polyphenol chemistry is involved in the adaptation to these environmental stressors. For example, the polymerization of catechins, resulting from leucoanthocyanidins/anthocyanidins submitted to reductive reactions, produces condensed tannins, which have an important role in defending plants against viruses, bacteria, fungi, insects, and herbivores [26,33,34].

## 2. Plant Phenolics and Their Role in Defense against Environmental Stresses

Environmental constraints such as drought, heat, salinity, cold, high light/UV-B, heavy metals, air pollution, nutritional deficiency, insect pests, and pathogens result in a harmful impact on plant growth and yield under field conditions [35–37]. Therefore, to cope with these conditions, plants must promptly identify environmental stresses and then activate defense responses. Environmental stress in plants induces changes in growth conditions, altering or disrupting their metabolic homeostasis. In these conditions, plant metabolism must be modified to make it possible to produce compounds necessary to cope with the stress. Such an adjustment of the metabolic pathways is usually referred to as acclimation. Changes of cellular and molecular activities represent plant strategies of adaptation to stress [38,39].

Higher plants accumulate a very large number of different (poly)phenolic structures that are believed to act as defense compounds against abiotic and biotic stresses [35,40]. Both constitutive and induced defenses are involved in the optimal protection of a plant against environmental stressors [41]. To understand and improve plants' stress responses and tolerances, researchers have focused on the signaling perception, transcriptional regulation, and expression of functional proteins in the stress response mechanisms. The accumulation of small molecules with antioxidative activity has often been discussed with respect to their role in mitigating the accumulation of reactive oxygen species (ROS) induced by stresses.

In the natural environment, plants come across several pests and pathogens. Plant defense toward potential pathogens includes both the rapid strengthening of pre-existing physical and chemical barriers and/or the *de novo* synthesis of a large number of defensive compounds through the induction of gene expression. The successful defense of a plant results in the restriction of fungal growth, which is usually caused by different defensive responses, such as the production of the so-called "phytoalexins" and pathogen-related proteins, and the accumulation of phenolic substances in the cell wall [42–46]. As far as pest attack is concerned, it should be stressed that the chemical composition of plant tissues is the main factor, together with physical factors, that influences insect acceptance or rejection of the plant as food. Phenolics also prevent insect oviposition on the host plant, as well as larval growth. It is well studied, for example, that flavonoids negatively influence the growth and development of various insects [47–49]. Tannins also may have a negative effect on insect growth due to their astringent taste, their ability to produce complex proteins, thus reducing digestibility, and their ability to act as enzyme inactivators. Recent papers [50–55] dealing with tannin oxidation in insects suggest that these oxidation reactions should also be considered as a plant defense mechanism [15]. The production of chemical defenses is expensive for plants due to the energy needed for their biosynthesis. To save these costs plants can produce chemical defenses just after an initial attack by a pathogen or insect. However, this strategy may not be effective if the attack is rapid and severe. Thus, plants exposed to frequent attacks invest resources in constitutive defenses, while plants that are subjected to rare attacks can rely on induced defenses [41,56,57].

Light is a fundamental important environmental signal regulating plant development and gene expression [58]. Elevated UV-B radiation that can be a consequence of ozone depletion has pleiotropic effects on plant life [59,60]. The most common effects are plant growth reductions and increased quantities of phenolic compounds in plant tissues [61]. Indeed, as for many abiotic stresses, ROS production is involved in UV radiation stress. A general strategy adopted by plants is to scavenge ROS using both enzymatic and nonenzymatic scavengers such as phenolic compounds [62,63].

Phenolic accumulation is induced by UV-B activation of the phenolic biosynthetic pathway. The presence of increased levels of phenolics in the epidermal cells results in hampering UV-B penetration, thus protecting the photosynthetically active tissues [64].

Both the primary and secondary metabolism of higher plants are influenced by mineral nutrition. In most terrestrial ecosystems, plant growth is nitrogen (N)-limited, but phosphorus (P)-limitation also occurs frequently. In these conditions, high concentrations of phenolics in tissues of low-productivity species growing at infertile sites are observed [65,66]. Broadly, it was observed that low-productivity species have higher amounts of secondary compounds than high-productivity species. Species growing in nutrient-poor habitats often have traits that lead to high nutrient retention and high levels of secondary metabolites, which have a defense role against herbivores and pathogens [67–70]. Deficiencies of essential elements (such as N, P and potassium (K)) can increase the amounts of phenolics in plant tissues either as existing pools or by inducing their *de novo* synthesis [71–73]. Barley plants grown under nitrogen deficiency conditions showed lower biomass, while leaf levels of soluble phenolics increased [74]. Iron deficiency induced increased amounts of phenolic acids in root exudates of non-graminaceous monocots and dicots [75–77]. An increased amount of anthocyanins is recognized as a consequence of P limitation. Anthocyanin over-accumulation lowers the accumulation of ROS *in vivo* under oxidative and drought stress [78]. As a consequence of P limitation, the content of phenylpropanoids and flavonoids resulted in increased *Arabidopsis thaliana* roots and shoots. The overexpression of MYB transcription factors PAP1/MYB75 and/or PAP2/MYB90 led plants to increase the content of anthocyanins and glycosides of quercetin and kaempferol [79,80]. This indicates that PAP1 and PAP2 have a role in increasing phenolics during P limitation [70,81,82].

Different hypotheses, such as the carbon-nutrient balance hypothesis and the growth-differentiation balance hypothesis, have been considered in order to explain the influence of nutrient deficiency on secondary phenolic metabolism. These hypotheses affirm that carbon skeletons synthesized by photosynthesis are dynamically used for growth (primary metabolism) or defense (secondary metabolism). Because allocation for plant growth and defense can take place at the same time in plants, these hypotheses suggest that secondary metabolism utilizes extra carbon skeletons when growth is more limited than photosynthesis (e.g., due to mineral element deficiencies) [57,67,83–85].

Low temperatures are another important plant abiotic stress. Lower temperatures alter the membrane structure, also affecting the activity of membrane-bound enzymes. An excessive production of ROS can be associated with chilling and this has deleterious effects on membranes. Moreover, low temperatures reduce scavenging enzyme activities, impairing the whole antioxidant plant response. In these conditions, some plants can adapt by modifying the membrane composition and activating oxygen-scavenging systems [86–88]. Low temperature conditions also determine the increased production of phenolics, which exert antioxidant activity in chilled tissues. An enhancement of phenylpropanoid metabolism is induced in plant tissues when temperatures decrease below a certain threshold value [15,89,90]. Low, non-freezing temperature stress induces an increase in phenylalanine ammonia-lyase and chalcone synthase activities, as well as the activation of a number of genes involved in phenolic metabolism [91]. Anthocyanins are believed to accumulate in leaves and stems of *Arabidopsis thaliana* in response to low temperatures [92–94]. Christie *et al.* [95] show that an increase in anthocyanin and mRNA abundance in the sheaths of maize seedlings are positively related with the severity and duration of the cold.

Finally, transition metals also cause oxidative stress in plants. Once again, transition metals most likely promote the formation of hydroxyl radical production. Available data suggest that heavy metals such as copper and cadmium, if they are not detoxified soon enough, may activate various reactions that, by disrupting cell redox control, lead to the inhibition of plant growth, the stimulation of secondary metabolism, and lignin deposition [96].

### 3. Costs of Resistance

Plant growth and development are dependent on the availability of essential environmental resources such as light, water, and nutrients. Usually, plants have to find a balance in the allocation of these resources to various physiological functions, such as growth and defense. Allocation theory in plant physiology assumes that plants have a limited supply of essential resources, which they must split between different competing physiological functions, such as growth, maintenance, and reproduction. These functions are mutually exclusive, since allocation to one function directly results in a decrease in the allocation to other functions, and consequently, an optimal pattern of allocation will exist. This multiple use of limited resources creates resource allocation trade-offs. It has been speculated that the process of allocation and trade-offs between various activities and functions must have been improved by natural selection. Because of these trade-offs between a plant's various functions, the concept of costs and benefits helps explain allocation patterns at both the physiological and evolutionary level [97]. External resources from the environment are devoted to internal needs, including growth, survival, and reproduction, as well as to physiological and genetic mechanisms of acclimation and genetic adaptation to the environment. Such a balance is continuously threatened by the occurrence of abiotic and biotic stress conditions. Hence, plants have also to devote a number of their resources to stress defense [15,98–101].

Plant defensive traits are costly for plants because of the energy needed for the biosynthesis of defensive compounds [84,102–104]. Hence, plants could struggle with the choice of allocating resources to different competing needs, creating possible trade-offs, *i.e.*, promoting some functions and neglecting others as an inverse relationship. Much research has been carried out for quantifying these costs in plants, *i.e.*, to link an evaluation of plant performance (in terms of growth rate) with levels of defense-related metabolites. Zangerl *et al.* [105] investigated the effects of the stress-induced defensive furanocoumarins on plant growth over a four-week period in wild parsnip. They found that total biomass and root biomass were reduced by 8.6% and 14%, respectively, in plants that had 2% of their leaf area removed compared to intact plants. At the same time, they also found an increase in furanocoumarin production. Pavia *et al.* [106] investigated the balance between phlorotannin production and plant growth by measuring phlorotannin content and annual growth in *Ascophyllum nodosum*. These authors found a significant negative correlation between phlorotannin content and plant growth. In good agreement with these data, allocation theory expects a trade-off mechanism between plant growth and defense needs, which allocates carbon between the primary and secondary metabolism, and that, in turn, provides the plant with an adequate adaptation mechanism against environmental stresses [56,84,97,98,107–114].

Primary metabolism provides carbon skeletons for the biosynthesis of phenolic metabolites (Figure 1), which are involved in several functions in signaling and defense against abiotic and biotic stress. Primary metabolism needs large amounts of the available plant resources. Therefore, when the growth rate is high, the production of phenolic compounds could be impaired by the shortage of substrates [115]. Plants producing defense compounds need to devote their limited resources to survival functions, being forced to make the choice between growing and defending, thus diverting carbon skeletons from the primary to secondary metabolism [84,98]. Therefore, plant metabolism must possess adequate flexibility to adapt to changes during development and to face environmental challenges. To this purpose, several mechanisms can be involved, including the alteration of enzyme kinetics as a reaction to metabolite level and/or induced gene transcription [116–121].

The “growth *vs.* defense” allocation dilemma has gained great interest in plant ecophysiology, even if specific plant choices that are the result of adaptation to particular environmental conditions are not definitely comprised [84,122–126]. The plant responses to environmental stress include biochemical and molecular mechanisms by which plants recognize and transfer the signals to cellular machinery, thus triggering adaptive reactions. Investigating mechanisms of stress signal transduction is greatly important in developing strategies for improving crop stress tolerance [15,127–129].

An increased level of phenolic metabolites in plant tissues is a peculiar trait of plant stress. Quantitative (pre-existing phenolics) and qualitative (induced phenolics, *de novo* synthesis) changes in phenolic composition confer to plants' various physiological functions that are useful for adapting to environmental disturbances [42,70,92,93,116,130–140]. Indeed, it must be stressed that the enhanced production comes from the enhanced activity of the enzymes involved in the phenolic pathway, including phenylalanine ammonia lyase and chalcone synthase. In addition, the enzyme activity of PEP (phosphoenolpyruvate)-carboxylase is enhanced, and this suggests a reallocation from sucrose production to defensive metabolite production [15,98,101,141–148].

What about the link between environmental stress and adaptive responses of plants to stress? Lattanzio *et al.* [115] suggest a scheme (Figure 2), which combines the amino acid proline, which is known to be induced by stress, with energy transfer to phenylpropanoid biosynthesis via the oxidative pentose phosphate pathway (OPPP) [149]. In plant tissues, an accumulation of free proline can be induced by many biotic and abiotic stresses. In this regard, it has also been suggested that the level of proline induced by stress conditions could be mainly mediated through the influence of its synthesis and degradation on cellular metabolism [115,150–153]. Most published papers have supported the role of proline as a mediator of osmotic imbalance, a free radical scavenger, and a source of reducing power. Proline also protects enzymes and membranes during changes of environmental conditions [154–156]. Proline action is also typical of a signaling molecule modulating cell physiology by inducing the expression of specific genes necessary for the plant stress response [157]. Moreover, it must be emphasized that stressed plants are often subjected to an excessive exposure to light, more than is needed for photosynthesis. When this occurs, the reduced regeneration of NADP<sup>+</sup> during photosynthetic carbon fixation results in cellular redox imbalance. Some studies suggest that a stress-induced increase in the transfer of reducing equivalents into the proline synthesis and degradation cycle should permit sensitive regulation of cellular redox potential in cytosol by enhancing the NADP<sup>+</sup>/NADPH ratio. The increased NADP<sup>+</sup>/NADPH ratio possibly enhances the OPPP activity, providing precursors required for the increased demand of phenolic metabolites to be produced during stress [151,155]. The alternating oxidation of NADPH by proline synthesis and the reduction of NADP<sup>+</sup> by the two oxidative steps of the OPPP serve to link both pathways, and this allows the maintenance of the high speed of proline production during stress.

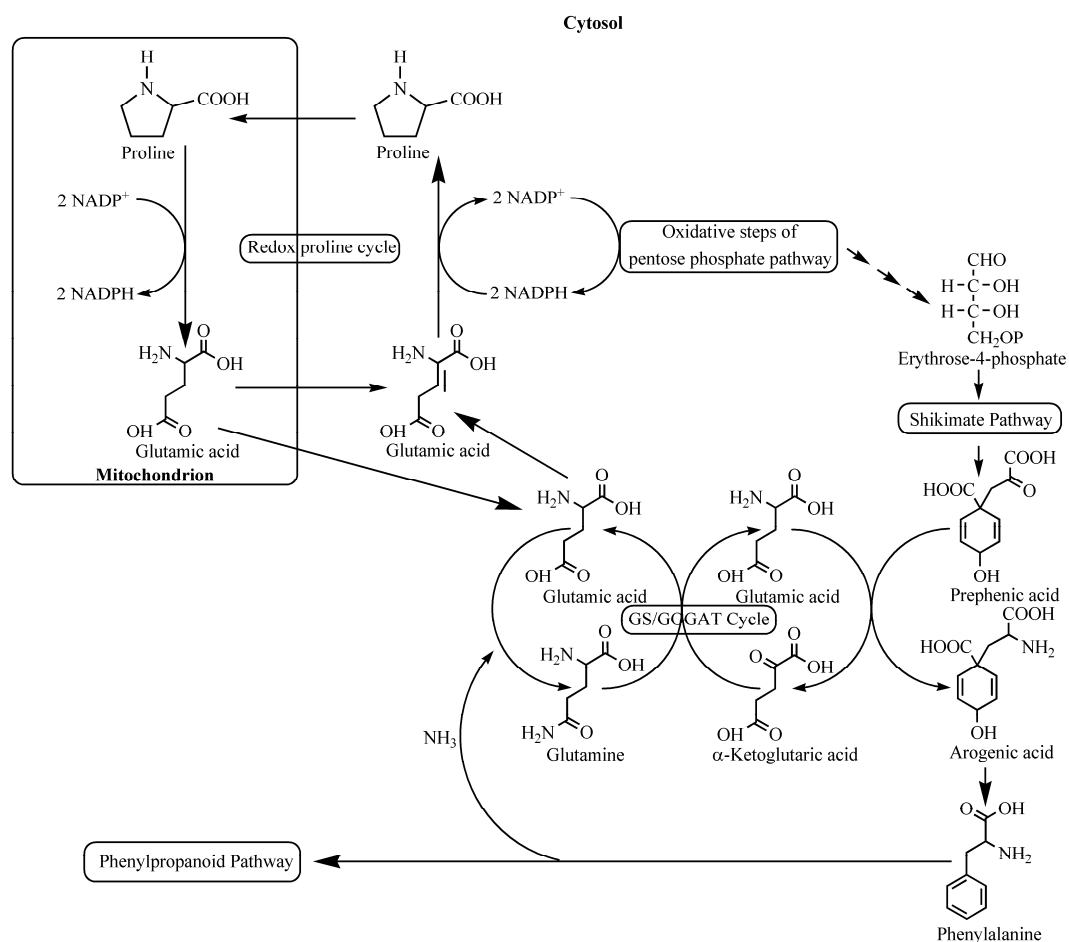
#### 4. Nutritional Stress Induces Supply Pathways from Primary Metabolism to Phenolic Secondary Product Formation

In plant tissues, increased amounts of phenolics observed under environmental stress can be considered both a common response of plant adaptation to stressful conditions, improving evolutionary fitness, and a way of channeling and storing carbon skeletons produced by photosynthesis during periods when plant growth is curtailed. The induction gene expression of phenolic metabolite pathways by biotic and abiotic stress is often acted by signaling molecules such as salicylic acid and jasmonic acid [3,14,15,158–160].

Both the OPPP and Calvin cycle can provide carbon skeletons in the form of erythrose-4-phosphate, which, together with glycolysis-derived phosphoenolpyruvate, acts as a precursor for phenylpropanoid metabolism via the shikimic acid pathway (Figure 1). In addition, it has been suggested that OPPP provides reducing equivalents to be used for the biosynthesis of phenolic compounds. Furthermore, OPPP activity results are enhanced when carbon flux into the phenylpropanoid pathway is also enhanced [115,161–163].

Lattanzio *et al.* [115] studied the influence of stress-induced synthesis of defensive phenolics on the growth of oregano (*Origanum vulgare* L.) shoots grown on Murashige and Skoog medium (MS) or half-strength MS medium. The growth rate and total phenolic content were shown to be significantly negatively correlated. Nutritional deficiency decreased the fresh biomass of oregano shoots (–40%) in comparison with the control (MS). On the contrary, nutritional stress induced a significant increase of both the total phenolic content (+120%) and rosmarinic acid, the most representative phenolic

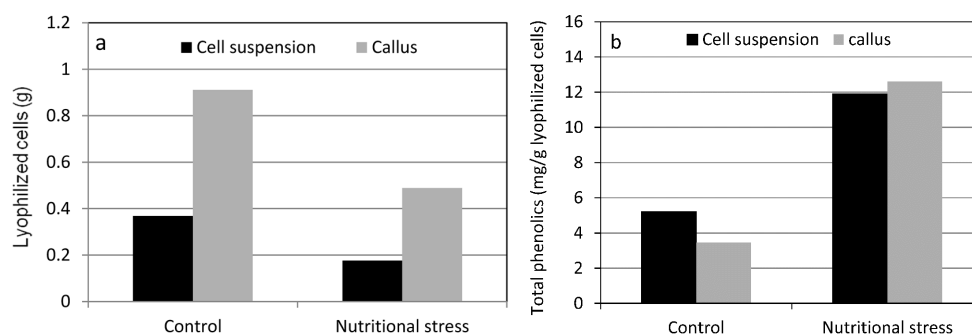
compound in oregano shoot extracts (+158%). The intracellular free proline content was also found increased (+31%). It should be noted that this moderate increase of endogenous proline in stressed tissues could be related to its consumption in increasing the net flux through the proline cycle (see Figure 2). Figure 2 also suggests a link between elicited proline and increased phenolic metabolism via the replacement of the NADP<sup>+</sup> delivery to OPPP which, successively, provides NADPH and carbon skeletons in the phenylpropanoid pathway [162,164–166].



**Figure 2.** Relationships between primary and secondary metabolism and role of endogenous proline in stimulating phenylpropanoid pathway. GS, glutamine synthetase; GOGAT, glutamate synthase (redrawn from [115] with permission of Elsevier).

Similar results have been observed when callus and cell suspension cultures of artichoke (*Cynara cardunculus* L. subsp. *scolymus* (L.) Hayek) subcultivated in Gamborg B5 medium (control) or in half-strength Gamborg B5 medium (nutritional stress) have been used as a model system. Both callus and cell suspension cultures suffered relevant changes when subjected to nutritional stress: they accumulated secondary metabolites and, meanwhile, their growth was negatively affected by stress conditions. Figure 3 shows the existence of a negative correlation between the growth rate (Figure 3a) and total phenolic content (Figure 3b) in cell cultures of artichoke. The growth rate of stressed cell suspension cultures was reduced by 52% compared to the non-stressed control. In contrast, the total phenolic content was enhanced by nutrient deficiency by 2.3-fold compared to the control level after a 30-day treatment. The same results were observed with artichoke callus cultures. Following nutrient deficiency, the growth of callus cultures was reduced by 47% compared to the control and this reduction seemed to be related to an energetic drain involved in generating the increased level of phenolic metabolites (3.6-fold greater than the control level) which diverts resources

from the biomass production. This evidence confirms the theoretical predictions that a trade-off exists between growth rate and defensive secondary metabolite investment when plant cells are in low-resource habitats [78,167]. Again, in order to understand the biochemical levels of regulatory mechanisms that control carbon fluxes between the primary and secondary metabolism, the role of proline, which figures prominently in most stress-mediated responses [115,168,169], has been also considered. The analysis of free proline content in cultivated artichoke cells shows an increase in proline level (by 38%–50% compared to the control) in response to nutritional stress. As already hypothesized for stressed oregano shoots, once again, it can be assumed that the observed increase of proline in artichoke cells subjected to nutrient deficiency could be explained by its rapid utilization in the proline redox cycle (see Figure 2).



**Figure 3.** Response of artichoke cells to nutrient deficiency. Cell growth (a) and total phenolic content (b). Unpublished data.

Broadly, in case of limited resources, plants need a well-balanced trade-off which permits growth without excluding defense responses. Various hypotheses have been proposed in order to elucidate the influence of environmental constraints on the trade-off between growth and defensive compounds. Some authors propose that it is the possibility of a trade-off between growth and differentiation (*i.e.*, biosynthesis of natural products, including phenolics) [67,84,170,171]. An alternative model [172–174] suggests a competition between protein and phenylpropanoid synthesis for using of the precursor phenylalanine. Therefore, at a high growth rate the synthesis of proteins reduces the availability of phenylalanine or phenolic biosynthesis. However, this model does not explain whether the protein synthesis and the synthesis of phenolics use the same pool of phenylalanine, or two separate pools.

Nowadays, the theory that growth and defense interact within the plant and compete for limited resources is considered a well-established principle. Because there are trade-offs between a plant's various functions, the concept of costs and benefits helps explain allocation patterns at both the physiological and evolutionary levels. One trade-off implies that constitutive or induced defenses need resources that could otherwise be devoted to growth and development. Comparisons among species suggest that high levels of defensive compounds are associated with resource-limited environments. Species adapted to low-nutrient availability generally have higher defense allocations than species of resource-rich habitats. In conditions of nutrient deficiency, if plants maintain defensive compound levels as nutrient resources decline, then growth and other competing physiological processes may decrease [65,67,97,110,144,175–178]. Here, it must be stressed that the phenolic metabolism is not only a feature of normal development but can also be induced by environmental stress conditions. Any new knowledge concerning responses of plant cell systems to real-life obstacles will help to improve our understanding of how plants work and how their resistance and/or tolerance to environmental stresses can be improved. In addition, this new knowledge can help to understand biochemical and molecular levels of regulatory mechanisms [179].

The above data are consistent with a biochemical regulatory mechanism proposed by Lattanzio *et al.* [115] (Figure 2). After the application of a nutritional stress, the growth rate of cell and



tissue cultures is reduced and this effect can be related to an energetic drain that redirects resources from biomass production. At the same time, the imposed nutritional stress induces an increase of intracellular proline, which improves the tolerance to ROS produced by stressed cell and tissue cultures [180,181].

It should also highlight that the increased synthesis of proline maintains NAD(P)<sup>+</sup>/NAD(P)H ratios at values compatible with cell metabolism under normal conditions. This adjustment could be considered a metabolic response which elicits the signal transduction pathway between the perception of nutritional stress and the adaptive physiological response. In addition, the increased NADP<sup>+</sup>/NADPH ratio, caused by proline synthesis, increases the activity of the OPPP. Mitochondrial proline oxidation can also affect the OPPP by recycling glutamic acid into the cytosol to generate a proline redox cycle [151]. Finally, glutamic acid could also be used to recycle ammonium ions, generated in the reductive deamination of phenylalanine, by means of the glutamine synthetase and glutamate synthase (GS/GOGAT) cycle [182,183].

## 5. Concluding Remarks

The resources to be managed by plants are carbon, nutrient elements, water, and energy. Management here means the allocation of resources to fundamental functions and to acclimate to the environment. Noticeably, such forms of allocation imply that the plant must make decisions. These decisions depend both on the plant's current developmental and metabolic status and on the environmental circumstances. For survival, plants need to regulate various requirements by means of resource allocation, estimating different sources and drops in resource fluxes *versus* the constraints associated with them [101].

When resources are limited, plants with naturally slow growth are favored over those with fast growth rates; slow growth rates, in turn, promote large investments in defense compounds [98,184]. Plant phenolics are defensive compounds that often accumulate in vegetative tissues when plants are subjected to different types of stress conditions. Whether and how stress-induced phenolics divert carbon skeletons from the primary metabolism and act as stress-protective molecules have been a subject of debate. As previously stated, phenolic levels increase during stress since growth is inhibited more than photosynthesis. Therefore, the photosynthates produced are redirected to the secondary metabolism [81]. Alternatively (or in addition), it could be suggested [15] that a peculiar feature of plant metabolism is the flexibility that allows it to respond to the environmental changes through developmental changes: adaptation strategies to environmental stress are costly and this could result in growth limitations.

Results discussed in this review support the hypothesis that there is a trade-off between growth and defense in plant cells (tissue and cell cultures) and that the trade-off is mediated by resource availability. Data also suggest that nutritional stress and stress-induced phenolics are linked by a transduction pathway that involves: (i) the proline redox cycle; (ii) the stimulated oxidative pentose phosphate pathway; and, in turn, (iii) the reduced growth of callus and cell suspension cultures.

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## References

1. Fiehn, O. Metabolomics—The link between genotypes and phenotypes. *Plant Mol. Biol.* **2002**, *48*, 155–171. [[CrossRef](#)] [[PubMed](#)]
2. Wu, S.; Chappell, J. Metabolic engineering of natural products in plants; tools of the trade and challenges for the future. *Curr. Opin. Biotechnol.* **2008**, *19*, 145–152. [[CrossRef](#)] [[PubMed](#)]

3. Lattanzio, V. Phenolic Compounds: Introduction. In *Handbook of Natural Products*; Ramawat, K.G., Merillon, J.M., Eds.; Springer-Verlag: Berlin Heidelberg, Germany, 2013; pp. 1543–1580.
4. Wink, M. Plant breeding: Importance of plant secondary metabolites for protection against pathogens and herbivores. *Theor. Appl. Genet.* **1988**, *75*, 225–233. [[CrossRef](#)]
5. Pichersky, E.; Gang, D.R. Genetics and biochemistry of secondary metabolites in plants: An evolutionary perspective. *Trends Plant Sci.* **2000**, *5*, 439–445. [[CrossRef](#)]
6. Osbourn, A.E.; Qi, X.; Townsend, B.; Qin, B. Dissecting plant secondary metabolism—Constitutive chemical defences in cereals. *New Phytol.* **2003**, *159*, 101–108. [[CrossRef](#)]
7. Wink, M. Evolution of secondary metabolites from an ecological and molecular phylogenetic perspective. *Phytochemistry* **2003**, *64*, 3–19. [[CrossRef](#)]
8. Noel, J.P.; Austin, M.B.; Bomati, E.K. Structure-function relationships in plant phenylpropanoid biosynthesis. *Curr. Opin. Plant Biol.* **2005**, *8*, 249–253. [[CrossRef](#)] [[PubMed](#)]
9. Ornston, L.N.; Yeh, W.K. Origins of metabolic diversity: Evolutionary divergence by sequence repetition. *Proc. Natl. Acad. Sci. USA* **1979**, *76*, 3996–4000. [[CrossRef](#)] [[PubMed](#)]
10. Wink, M. *Biochemistry of Plant Secondary Metabolism*; Sheffield Academic Press: Sheffield, UK; CRC Press: Boca Raton, FL, USA, 1999.
11. Leheldt, C.; Shirley, A.M.; Meyer, K.; Ruegger, M.O.; Cusumano, J.C.; Viitanen, P.V.; Strack, D.; Chapple, C. Cloning of the *SNG1* gene of *Arabidopsis* reveals a role for a serine carboxypeptidase-like protein as an acyltransferase in secondary metabolism. *Plant Cell* **2000**, *12*, 1295–1306. [[CrossRef](#)] [[PubMed](#)]
12. Tauber, E.; Last, K.S.; Olive, P.J.; Kyriacou, C.P. Clock gene evolution and functional divergence. *J. Biol. Rhythms* **2004**, *19*, 445–458. [[CrossRef](#)] [[PubMed](#)]
13. Broun, P. Transcriptional control of flavonoid biosynthesis: A complex network of conserved regulators involved in multiple aspects of differentiation in *Arabidopsis*. *Curr. Opin. Plant Biol.* **2005**, *8*, 272–279. [[CrossRef](#)] [[PubMed](#)]
14. Do Nascimento, N.C.; Fett-Neto, A.G. Plant secondary metabolism and challenges in modifying its operation: An overview. In *Plant Secondary Metabolism Engineering—Methods and Application, Methods in Molecular Biology*; Fett-Neto, A.G., Ed.; Humana Press: New York, NY, USA, 2010; Volume 643, pp. 1–13.
15. Lattanzio, V.; Cardinali, A.; Linsalata, V. Plant phenolics: A biochemical and physiological perspective. In *Recent Advances in Polyphenols Research*; Cheyner, V., Sarni-Manchado, P., Quideau, S., Eds.; Wiley-Blackwell Publishing: Oxford, UK, 2012; Volume 3, pp. 1–39.
16. Robards, R.; Antolovich, M. Analytical chemistry of fruit bioflavonoids. A review. *Analyst* **1997**, *122*, 11R–34R. [[CrossRef](#)]
17. Harborne, J.B. Plant phenolics. In *Encyclopedia of Plant Physiology, New Series, Secondary Plant Products*; Bell, E.A., Charlwood, B.V., Eds.; Springer-Verlag: Berlin, Germany, 1980; Volume 8, pp. 329–402.
18. Lattanzio, V.; Kroon, P.A.; Quideau, S.; Treutter, D. Plant phenolics—Secondary metabolites with diverse functions. In *Recent Advances in Polyphenol Research*; Daayf, F., Lattanzio, V., Eds.; Wiley-Blackwell Publishing: Oxford, UK, 2008; Volume 1, pp. 1–35.
19. Swain, T. Evolution of flavonoid compounds. In *The Flavonoids*; Harborne, J.B., Mabry, T.J., Mabry, H., Eds.; Chapman & Hall: London, UK, 1975; pp. 1096–1138.
20. Boudet, A.M.; Graziana, A.; Ranjeva, R. Recent advances in the regulation of the prearomatic pathway. In *The Biochemistry of Plant Phenolics*; van Sumere, C.F., Lea, P.J., Eds.; Clarendon Press: London, UK, 1985; pp. 135–160.
21. Hrazdina, G.; Jensen, R.A. Spatial organization of enzymes in plant metabolic pathways. *Annu. Rev. Plant. Physiol. Plant Mol. Biol.* **1992**, *43*, 241–267. [[CrossRef](#)]
22. Hrazdina, G. Compartmentation in phenolic metabolism. *Acta Hortic.* **1994**, *381*, 86–96. [[CrossRef](#)]
23. Schmid, J.; Amrhein, N. Molecular organization of the shikimate pathway in higher plants. *Phytochemistry* **1995**, *39*, 737–749. [[CrossRef](#)]
24. Winkel-Shirley, B. Flavonoid biosynthesis: A colorful model for genetics, biochemistry, cell biology and biotechnology. *Plant Physiol.* **2001**, *126*, 485–493. [[CrossRef](#)] [[PubMed](#)]
25. Austin, M.B.; Noel, J.P. The chalcone synthase superfamily of type III polyketide synthases. *Nat. Prod. Rep.* **2003**, *20*, 79–110. [[CrossRef](#)] [[PubMed](#)]
26. Cheyner, V.; Comte, G.; Davies, K.M.; Lattanzio, V.; Martens, S. Plant phenolics: Recent advances on their biosynthesis, genetics, and ecophysiology. *Plant Physiol. Biochem.* **2013**, *72*, 1–20. [[CrossRef](#)] [[PubMed](#)]

27. Boudet, A.M. Evolution and current status of research in phenolic compounds. *Phytochemistry* **2007**, *68*, 2722–2735. [[CrossRef](#)] [[PubMed](#)]
28. Graham, L.E.; Cook, M.E.; Busse, J.S. The origin of plants: Body plan changes contributing to a major evolutionary radiation. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 4535–4540. [[CrossRef](#)] [[PubMed](#)]
29. Lowry, B.; Lee, D.; Hébant, C. The origin of land plants: A new look at an old problem. *Taxon* **1980**, *29*, 183–197. [[CrossRef](#)]
30. Gottlieb, O.R. Phytochemical evolution. *Rev. Acad. Pol. Sci. Ex. Fis. Nat.* **1986**, *16*, 39–45.
31. Hertweck, C. The biosynthetic logic of polyketide diversity. *Angew. Chem. Int. Ed.* **2009**, *48*, 4688–4716. [[CrossRef](#)] [[PubMed](#)]
32. McClure, J.W. Physiology and function of flavonoids. In *The Flavonoids*; Harborne, J.B., Mabry, T.J., Mabry, H., Eds.; Chapman & Hall: London, UK, 1975; pp. 970–1055.
33. Gottlieb, O.R. The role of oxygen in phytochemical evolution towards diversity. *Phytochemistry* **1989**, *28*, 2545–2558. [[CrossRef](#)]
34. Gottlieb, O.R.; Kaplan, M.A.C. Phytochemical evolution: The redox theory. *Nat. Prod. Lett.* **1993**, *2*, 171–176. [[CrossRef](#)]
35. Dixon, R.A.; Paiva, N.L. Stress-induced secondary metabolism. *Plant Cell* **1995**, *7*, 1085–1097. [[CrossRef](#)] [[PubMed](#)]
36. Atkinson, N.J.; Urwin, P.E. The interaction of plant biotic and abiotic stresses: From genes to the field. *J. Exp. Bot.* **2012**, *63*, 3523–3543. [[CrossRef](#)] [[PubMed](#)]
37. Suzuki, N.; Rivero, R.M.; Shulaev, V.; Blumwald, E.; Mittler, R. Abiotic and biotic stress combinations. *New Phytol.* **2014**, *203*, 32–43. [[CrossRef](#)] [[PubMed](#)]
38. Shulaev, V.; Cortes, D.; Miller, G.; Mittler, R. Metabolomics for plant stress response. *Physiol. Plant.* **2008**, *132*, 199–208. [[CrossRef](#)] [[PubMed](#)]
39. Ahuja, I.; de Vos, R.C.H.; Bones, A.M.; Hall, R.D. Plant molecular stress responses face climate change. *Trends Plant Sci.* **2010**, *15*, 664–674. [[CrossRef](#)] [[PubMed](#)]
40. Nakabayashi, R.; Saito, K. Integrated metabolomics for abiotic stress responses in plants. *Curr. Opin. Plant Biol.* **2015**, *24*, 10–16. [[CrossRef](#)] [[PubMed](#)]
41. Wittstock, U.; Gershenzon, J. Constitutive plant toxins and their role in defense against herbivores and pathogens. *Curr. Opin. Plant Biol.* **2002**, *5*, 300–307. [[CrossRef](#)]
42. Lattanzio, V.; Lattanzio, V.M.T.; Cardinali, A. Role of phenolics in the resistance mechanisms of plants against fungal pathogens and insects. In *Phytochemistry: Advances in Research*; Imperato, F., Ed.; Research Signpost: Trivandrum, India, 2006; pp. 23–67.
43. Somssich, I.E.; Bollmann, J.; Hahlbrock, K.; Kombrink, E.; Schulz, W. Differential early activation of defense-related genes in elicitor-treated parsley cells. *Plant Mol. Biol.* **1989**, *12*, 227–234. [[CrossRef](#)] [[PubMed](#)]
44. Somssich, I.E.; Wernert, P.; Kiedrowski, S.; Hahlbrock, K. *Arabidopsis thaliana* defense-related protein ELI3 is an aromatic alcohol:NADP<sup>+</sup> oxidoreductase. *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 14199–14203. [[CrossRef](#)] [[PubMed](#)]
45. Somssich, I.E.; Hahlbrock, K. Pathogen defense in plants—A paradigm of biological complexity. *Trends Plant Sci.* **1998**, *3*, 86–90. [[CrossRef](#)]
46. Ligterink, W.; Kroj, T.; zur Nieden, U.; Hirt, H.; Scheel, D. Receptor-mediated activation of a MAP kinase in pathogen defense of plants. *Science* **1997**, *276*, 2054–2057. [[CrossRef](#)] [[PubMed](#)]
47. Lattanzio, V.; Arpaia, S.; Cardinali, A.; di Venere, D.; Linsalata, V. Role of endogenous flavonoids in resistance mechanism of *Vigna* to aphids. *J. Agric. Food Chem.* **2000**, *48*, 5316–5320. [[CrossRef](#)] [[PubMed](#)]
48. Simmonds, M.S.J. Importance of flavonoids in insect-plant interactions: Feeding and oviposition. *Phytochemistry* **2001**, *56*, 245–252. [[CrossRef](#)]
49. Simmonds, M.S.J. Flavonoid-insect interactions: Recent advances in our knowledge. *Phytochemistry* **2003**, *64*, 21–30. [[CrossRef](#)]
50. Winkel-Shirley, B. Flavonoids in seeds and grains: Physiological function, agronomic importance and the genetics of biosynthesis. *Seed Sci. Res.* **1998**, *8*, 415–422.
51. Constabel, C.P.; Barbehenn, R. Defensive roles of polyphenol oxidase in plants. In *Induced Plant Resistance to Herbivory*; Schaller, A., Ed.; Springer Science + Business Media B.V.: New York, NY, USA, 2008; pp. 253–269.
52. Barbehenn, R.; Dukatz, C.; Holt, C.; Reese, A.; Martiskainen, O.; Salminen, J.-P.; Yip, L.; Tran, L.; Constabel, C.P. Feeding on poplar leaves by caterpillars potentiates foliar peroxidase action in their guts and increases plant resistance. *Oecologia* **2010**, *164*, 993–1004. [[CrossRef](#)] [[PubMed](#)]

53. Barbehenn, R.; Weir, Q.; Salminen, J.-P. Oxidation of ingested phenolics in the tree feeding caterpillar *Orygia leucostigma* depends on foliar chemical composition. *J. Chem. Ecol.* **2008**, *34*, 748–756. [[CrossRef](#)] [[PubMed](#)]
54. Barbehenn, R.V.; Jaros, A.; Lee, G.; Mozola, C.; Weir, Q.; Salminen, J.-P. Tree resistance to *Lymantria dispar* caterpillars: Importance and limitations of foliar tannin composition. *Oecologia* **2009**, *159*, 777–788. [[CrossRef](#)] [[PubMed](#)]
55. Barbehenn, R.V.C.; Jaros, A.; Lee, G.; Mozola, C.; Weir, Q.; Salminen, J.-P. Hydrolyzable tannins as “quantitative defenses”: Limited impact against *Lymantria dispar* caterpillars on hybrid poplar. *J. Insect Physiol.* **2009**, *55*, 297–304. [[CrossRef](#)] [[PubMed](#)]
56. Purrington, C.B. Costs of resistance. *Curr. Opin. Plant Biol.* **2000**, *3*, 305–308. [[CrossRef](#)]
57. Stamp, N. Out of the quagmire of plant defense hypotheses. *Q. Rev. Biol.* **2003**, *78*, 23–55. [[CrossRef](#)] [[PubMed](#)]
58. Christie, J.M.; Jenkins, G.I. Distinct UV-B and UV-A/Blue light signal transduction pathways induce chalcone synthase gene expression in *Arabidopsis* cells. *Plant Cell* **1996**, *8*, 1555–1567. [[CrossRef](#)] [[PubMed](#)]
59. Frohnmeyer, H.; Staiger, D. Ultraviolet-B radiation mediated responses in plants. Balancing damage and protection. *Plant Physiol.* **2003**, *133*, 1420–1428. [[CrossRef](#)] [[PubMed](#)]
60. Hectors, K.; Prinsen, E.; Coen, W.D.; Jansen, M.A.K.; Guisez, Y. *Arabidopsis thaliana* plants acclimated to low dose rates of ultraviolet B radiation show specific changes in morphology and gene expression in the absence of stress symptoms. *New Phytol.* **2007**, *175*, 255–270. [[CrossRef](#)] [[PubMed](#)]
61. Caldwell, M.M.; Ballaré, C.L.; Bornman, J.F.; Flint, S.D.; Bjorn, L.O.; Teramura, A.H.; Kulandaivelu, G.; Tevini, M. Terrestrial ecosystems, increased solar ultraviolet radiation and interactions with other climatic change factors. *Photochem. Photobiol. Sci.* **2003**, *2*, 29–38. [[CrossRef](#)] [[PubMed](#)]
62. Mittler, R.; Vanderauwera, S.; Gollery, M.; van Breusegem, F. Reactive oxygen gene network of plants. *Trends Plant Sci.* **2004**, *9*, 490–498. [[CrossRef](#)] [[PubMed](#)]
63. Grace, S.C.; Logan, B.A. Energy dissipation and radical scavenging by the plant phenylpropanoid pathway. *Philos. Trans. R. Soc. Lond. B* **2000**, *355*, 1499–1510. [[CrossRef](#)] [[PubMed](#)]
64. Mazza, C.A.; Boccalandro, H.E.; Giordano, C.V.; Battista, D.; Scopel, A.L.; Ballaré, C.L. Functional significance and induction by solar radiation of ultra-violet-absorbing sunscreens in field-grown soybean crops. *Plant Physiol.* **2000**, *122*, 117–125. [[CrossRef](#)] [[PubMed](#)]
65. Aerts, R.; Chapin, F.S., III. The mineral nutrition of wild plants revisited: A re-evaluation of processes and patterns. *Adv. Ecol. Res.* **2000**, *30*, 1–67.
66. Scheible, W.-R.; Morcuende, R.; Czechowski, T.; Fritz, C.; Osuna, D.; Palacios-Rojas, N.; Schindelasch, D.; Thimm, O.; Udvardi, M.K.; Stitt, M. Genome-wide reprogramming of primary and secondary metabolism, protein synthesis, cellular growth processes, and the regulatory infrastructure of *Arabidopsis* in response to nitrogen. *Plant Physiol.* **2004**, *136*, 2483–2499. [[CrossRef](#)] [[PubMed](#)]
67. Bryant, J.P.; Chapin, F.S., III; Klein, D.R. Carbon nutrient balance of boreal plants in relation to vertebrate herbivory. *Oikos* **1983**, *40*, 357–368. [[CrossRef](#)]
68. Niemann, G.J.; Pureveen, J.B.M.; Eijkel, G.B.H.; Poorter, H.; Boon, J.J. Differences in relative growth rate in 11 grasses correlate with differences in chemical composition as determined by pyrolysis mass spectrometry. *Oecologia* **1992**, *89*, 567–573. [[CrossRef](#)]
69. Poorter, H.; Bergkotte, M. Chemical composition of 24 wild species differing in relative growth rate. *Plant Cell Environ.* **1992**, *15*, 221–229. [[CrossRef](#)]
70. Lillo, C.; Lea, U.S.; Ruoff, P. Nutrient depletion as a key factor for manipulating gene expression and product formation in different branches of the flavonoid pathway. *Plant Cell Environ.* **2008**, *31*, 587–601. [[CrossRef](#)] [[PubMed](#)]
71. Haukioja, E.; Ossipov, V.; Koricheva, J.; Honkanen, T.; Larsson, S.; Lempa, K. Biosynthetic origin of carbon-based secondary compounds: Cause of variable responses of woody plants to fertilization? *Chemoecology* **1998**, *8*, 133–139. [[CrossRef](#)]
72. Kováčik, J.; Klejdus, B.; Bačkor, M.; Repčák, M. Phenylalanine ammonia-lyase activity and phenolic compounds accumulation in nitrogen-deficient *Matricaria chamomilla* leaf rosettes. *Plant Sci.* **2007**, *172*, 393–399. [[CrossRef](#)]
73. Glynn, C.; Herms, D.A.; Orians, C.M.; Hansen, R.C.; Larsson, S. Testing the growth-differentiation balance hypothesis: Dynamic responses of willows to nutrient availability. *New Phytol.* **2007**, *176*, 623–634. [[CrossRef](#)] [[PubMed](#)]

74. Mercure, S.A.; Daoust, B.; Samson, G. Causal relationship between growth inhibition, accumulation of phenolic metabolites, and changes of UV-induced fluorescences in nitrogen-deficient barley plants. *Can. J. Bot.* **2004**, *6*, 815–821. [[CrossRef](#)]
75. Jin, C.W.; You, G.Y.; He, Y.F.; Tang, C.X.; Wu, P.; Zheng, S.J. Iron deficiency induced secretion of phenolics facilitates the reutilization of root apoplastic iron in red clover. *Plant Physiol.* **2007**, *144*, 278–285. [[CrossRef](#)] [[PubMed](#)]
76. Jin, C.W.; You, G.Y.; Zheng, S.J. The iron deficiency-induced phenolics secretion plays multiple important roles in plant iron acquisition underground. *Plant Signal. Behav.* **2008**, *3*, 60–61. [[CrossRef](#)] [[PubMed](#)]
77. Vigani, G.; Zocchi, G.; Bashir, K.; Phillipar, K.; Briat, J.F. Cellular iron homeostasis and metabolism in plants. *Front. Plant Sci.* **2013**, *4*, 6–8. [[CrossRef](#)] [[PubMed](#)]
78. Nakabayashi, R.; Yonekura-Sakaibara, K.; Urano, K.; Suzuki, M.; Yamada, Y.; Nishizawa, T.; Matsuda, F.; Kojima, M.; Sakakibara, H.; Shinozaki, K.; *et al.* Enhancement of oxidative and drought tolerance in *Arabidopsis* by overaccumulation of antioxidant flavonoids. *Plant J.* **2014**, *77*, 367–379. [[CrossRef](#)] [[PubMed](#)]
79. Tohge, T.; Nishiyama, Y.; Hirai, M.Y.; Yano, M.; Nakajima, J.-I.; Awazuhara, M.; Inoue, E.; Takahashi, H.; Goodenowe, D.B.; Kitayama, M.; *et al.* Functional genomics by integrated analysis of metabolome and transcriptome of *Arabidopsis* plants over-expressing an MYB transcription factor. *Plant J.* **2005**, *42*, 218–235. [[CrossRef](#)] [[PubMed](#)]
80. Morcuende, R.; Bari, R.; Gibon, Y.; Zheng, W.; Pant, B.D.; Blasing, O.; Usadel, B.; Czechowski, T.; Udvardi, M.K.; Stitt, M.; *et al.* Genome-wide reprogramming of metabolism and regulatory networks of *Arabidopsis* in response to phosphorus. *Plant Cell Environ.* **2007**, *30*, 85–112. [[CrossRef](#)] [[PubMed](#)]
81. Pant, B.-D.; Pant, P.; Erban, A.; Huhman, D.; Kopka, J.; Scheible, W.-R. Identification of primary and secondary metabolites with phosphorus status-dependent abundance in *Arabidopsis*, and of the transcription factor PHR1 as a major regulator of metabolic changes during phosphorus limitation. *Plant Cell Environ.* **2015**, *38*, 172–187. [[CrossRef](#)] [[PubMed](#)]
82. Rubio, V.; Linhares, F.; Solano, R.; Martin, A.C.; Iglesias, J.; Leyva, A.; Paz-Ares, J. A conserved MYB transcription factor involved in phosphate starvation signaling both in vascular plants and in unicellular algae. *Genes Dev.* **2001**, *15*, 2122–2133. [[CrossRef](#)] [[PubMed](#)]
83. Liakopoulos, G.; Karabourniotis, G. Boron deficiency and concentrations and composition of phenolic compounds in *Olea europaea* leaves: A combined growth chamber and field study. *Tree Physiol.* **2005**, *25*, 307–315. [[CrossRef](#)] [[PubMed](#)]
84. Herms, D.A.; Mattson, W.J. The dilemma of plants: To grow or defend. *Q. Rev. Biol.* **1992**, *67*, 283–335. [[CrossRef](#)]
85. Hamilton, J.G.; Zangerl, A.R.; DeLucia, E.H.; Berenbaum, M.R. The carbon-nutrient balance hypothesis: Its rise and fall. *Ecol. Lett.* **2001**, *4*, 86–95. [[CrossRef](#)]
86. Oh, M.-M.; Trick, H.N.; Rajashekar, C.B. Secondary metabolism and antioxidants are involved in environmental adaptation and stress tolerance in lettuce. *J. Plant Physiol.* **2009**, *166*, 180–191. [[CrossRef](#)] [[PubMed](#)]
87. Lütz, C. Cell physiology of plants growing in cold environments. *Protoplasma* **2010**, *244*, 53–73. [[CrossRef](#)] [[PubMed](#)]
88. Airaki, M.; Leterrier, M.; Mateos, R.M.; Valderrama, R.; Chaki, M.; Barroso, J.B.; del Rio, L.A.; Palma, J.M.; Corpas, F.J. Metabolism of reactive oxygen species and reactive nitrogen species in pepper (*Capsicum annuum* L.) plants under low temperature stress. *Plant Cell Environ.* **2012**, *35*, 281–295. [[CrossRef](#)] [[PubMed](#)]
89. Lattanzio, V.; van Sumere, C.F. Changes in phenolic compounds during the development and cold storage of artichoke (*Cynara scolymus* L.) heads. *Food Chem.* **1987**, *24*, 37–50. [[CrossRef](#)]
90. Lattanzio, V.; di Venere, D.; Linsalata, V.; Bertolini, P.; Ippolito, A.; Salerno, M. Low temperature metabolism of apple phenolics and quiescence of *Phlyctaena vagabunda*. *J. Agric. Food Chem.* **2001**, *49*, 5817–5821. [[CrossRef](#)] [[PubMed](#)]
91. Stefanowska, M.; Kuras, M.; Kacperska, A. Low temperature induced modifications in cell ultrastructure and localization of phenolics in winter oilseed rape (*Brassica napus* L. var *oleifera* L.) leaves. *Ann. Bot.* **2002**, *90*, 637–645. [[CrossRef](#)] [[PubMed](#)]
92. Leyva, A.; Jarillo, J.A.; Salinas, J.; Martinez-Zapater, J.M. Low temperature induces the accumulation of phenylalanine ammonia-lyase and chalcone synthase mRNAs of *Arabidopsis thaliana* in a light-dependent manner. *Plant Physiol.* **1995**, *108*, 39–46. [[PubMed](#)]
93. Chalker-Scott, L. Environmental significance of anthocyanins in plant stress responses. *Photochem. Photobiol.* **1999**, *70*, 1–9. [[CrossRef](#)]

94. Solecka, D.; Boudet, A.M.; Kacperska, A. Phenylpropanoid and anthocyanin changes in low-temperature treated oilseed rape leaves. *Plant Physiol. Biochem.* **1999**, *37*, 491–496. [[CrossRef](#)]
95. Christie, P.J.; Alfenito, M.R.; Walbot, V. Impact of low-temperature stress on general phenylpropanoid and anthocyanin pathways: Enhancement of transcript abundance and anthocyanin pigmentation in maize seedlings. *Planta* **1994**, *194*, 541–549. [[CrossRef](#)]
96. Schützendübel, A.; Polle, A. Plant responses to abiotic stresses: Heavy metal-induced oxidative stress and protection by mycorrhization. *J. Exp. Bot.* **2002**, *53*, 1351–1365. [[CrossRef](#)] [[PubMed](#)]
97. Bazzaz, F.A.; Chiariello, N.R.; Coley, P.D.; Pitelka, L.F. Allocating resources to reproduction and defense. *BioScience* **1987**, *37*, 58–67. [[CrossRef](#)]
98. Coley, P.D.; Bryant, J.P.; Chapin, F.S., III. Resource availability and plant antiherbivore defense. *Science* **1985**, *230*, 895–899. [[CrossRef](#)] [[PubMed](#)]
99. Bazzaz, F.A.; Grace, J. *Plant Resource Allocation*; Academic Press: London, UK, 1997.
100. Bazzaz, F.A.; Ackerly, D.D.; Reekie, E.G. Reproductive allocation in plants. In *Seeds: The Ecology of Regeneration in Plant Communities*; Fenner, M., Ed.; CABI Publishing: Wallingford, UK, 2000; pp. 1–30.
101. Matyssek, R.; Schnyder, H.; Oßwald, W.; Ernst, D.; Munch, J.C.; Pretzsch, H. *Growth and Defence in Plants, Ecological Studies Volume 220*; Springer-Verlag: Berlin Heidelberg, Germany, 2012.
102. Heil, M.; Hilpert, A.; Kaiser, W.; Linsenmair, E. Reduced growth and seed set following chemical induction of pathogen defence: Does systemic acquired resistance (SAR) incur allocation costs? *J. Ecol.* **2000**, *88*, 645–654. [[CrossRef](#)]
103. Heil, M.; Baldwin, I.T. Fitness costs of induced resistance: Emerging experimental support for a slippery concept. *Trends Plant Sci.* **2002**, *7*, 61–67. [[CrossRef](#)]
104. Strauss, S.Y.; Rudgers, J.A.; Lau, J.A.; Irwin, R.E. Direct and ecological costs of resistance to herbivory. *Trends Ecol. Evol.* **2002**, *17*, 278–284. [[CrossRef](#)]
105. Zangerl, A.R.; Arntz, A.M.; Berenbaum, M.R. Physiological price of an induced chemical defense: Photosynthesis, respiration, biosynthesis, and growth. *Oecologia* **1997**, *109*, 433–441. [[CrossRef](#)]
106. Pavia, H.; Toth, G.; Aberg, P. Trade-offs between phlorotannin production and annual growth in natural populations of the brown seaweed *Ascophyllum nodosum*. *J. Ecol.* **1999**, *87*, 761–771. [[CrossRef](#)]
107. Chapin, F.S., III; Bloom, A.J.; Field, C.B.; Waring, R.H. Plant responses to multiple environmental factors. *BioScience* **1987**, *37*, 49–57. [[CrossRef](#)]
108. Brown, J.K.M. A cost of disease resistance: Paradigm or peculiarity? *Trends Genet.* **2003**, *19*, 667–671. [[CrossRef](#)] [[PubMed](#)]
109. Burdon, J.J.; Thrall, P.H. The fitness costs to plants of resistance to pathogens. *Genome Biol.* **2003**, *4*, 227.1–227.3. [[CrossRef](#)] [[PubMed](#)]
110. Siemens, D.H.; Lischke, H.; Maggiulli, N.; Schürch, S.; Roy, B.A. Cost of resistance and tolerance under competition: The defense-stress benefit hypothesis. *Evol. Ecol.* **2003**, *17*, 247–263. [[CrossRef](#)]
111. Dietrich, R.; Ploss, K.; Heil, M. Growth responses and fitness costs after induction of pathogen resistance depend on environmental conditions. *Plant Cell Environ.* **2005**, *28*, 211–222. [[CrossRef](#)]
112. Hernández, I.; van Breusegem, F. Opinion on the possible role of flavonoids as energy escape valves: Novel tools for nature’s Swiss army knife. *Plant Sci.* **2010**, *179*, 297–301. [[CrossRef](#)]
113. Selmar, D.; Kleinwächter, M. Influencing the product quality by deliberately applying drought stress during the cultivation of medicinal plants. *Ind. Crop. Prod.* **2013**, *42*, 558–566. [[CrossRef](#)]
114. Kleinwächter, M.; Selmar, D. New insights explain that drought stress enhances the quality of spice and medicinal plants: Potential applications. *Agron. Sustain. Dev.* **2015**, *35*, 121–131. [[CrossRef](#)]
115. Lattanzio, V.; Cardinali, A.; Ruta, C.; Morone Fortunato, I.; Lattanzio, V.M.T.; Linsalata, V.; Cicco, N. Relationship of secondary metabolism to growth in oregano (*Origanum vulgare* L.) shoot cultures under nutritional stress. *Environ. Exp. Bot.* **2009**, *65*, 54–62. [[CrossRef](#)]
116. Logemann, E.; Tavernaro, A.; Schulz, W.; Somssich, I.E.; Hahlbrock, K. UV light selectively co-induces supply pathways from primary metabolism and flavonoid secondary product formation in parsley. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 1903–1907. [[CrossRef](#)] [[PubMed](#)]
117. Henkes, S.; Sonnewald, U.; Badur, R.; Flachmann, R.; Stitt, M. A small decrease of plastid transketolase activity in antisense tobacco transformants has dramatic effects on photosynthesis and phenylpropanoid metabolism. *Plant Cell* **2001**, *13*, 535–551. [[CrossRef](#)] [[PubMed](#)]

118. Nakane, E.; Kawakita, K.; Doke, N.; Yoshioka, H. Elicitation of primary and secondary metabolism during defense in the potato. *J. Gen. Plant. Pathol.* **2003**, *69*, 378–384. [[CrossRef](#)]
119. Lloyd, J.C.; Zakhleniuk, O.V. Responses of primary and secondary metabolism to sugar accumulation revealed by microarray expression analysis of the *Arabidopsis* mutant, *pho3*. *J. Exp. Bot.* **2004**, *55*, 1221–1230. [[CrossRef](#)] [[PubMed](#)]
120. Leser, C.; Treutter, D. Effects of nitrogen supply on growth, contents of phenolic compounds and pathogen (scab) resistance of apple trees. *Physiol. Plant.* **2005**, *123*, 49–56. [[CrossRef](#)]
121. Fritz, C.; Palacios-Rojas, N.; Feil, R.; Stitt, M. Regulation of secondary metabolism by the carbon-nitrogen status in tobacco: Nitrate inhibits large sectors of phenylpropanoid metabolism. *Plant J.* **2006**, *46*, 533–548. [[CrossRef](#)] [[PubMed](#)]
122. Leone, M.; Keller, M.M.; Ballaré, C.L. To grow or defend? Low red: Far-red ratios reduce jasmonate sensitivity in *Arabidopsis* seedlings by promoting DELLA degradation and increasing JAZ10 stability. *New Phytol.* **2014**, *204*, 355–367. [[CrossRef](#)] [[PubMed](#)]
123. Agrawal, A. Benefits and costs of induced plant defense for *Lepidium virginicum* (Brassicaceae). *Ecology* **2000**, *81*, 1804–1813. [[CrossRef](#)]
124. Cipollini, D. Stretching the limits of plasticity: Can a plant defend against both competitors and herbivores? *Ecology* **2004**, *85*, 28–37. [[CrossRef](#)]
125. Izaguirre, M.M.; Mazza, C.A.; Biondini, M.; Baldwin, I.T.; Ballaré, C.L. Remote sensing of future competitors: Impacts on plant defenses. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 7170–7174. [[CrossRef](#)] [[PubMed](#)]
126. Ballaré, C.L. Illuminated behaviour: Phytochrome as a key regulator of light foraging and plant anti-herbivore defence. *Plant Cell Environ.* **2009**, *32*, 713–725. [[CrossRef](#)] [[PubMed](#)]
127. Xiong, L.; Schumaker, K.S.; Zhu, J.K. Cell signaling during cold, drought, and salt stress. *Plant Cell* **2002**, *14*, S165–S183. [[PubMed](#)]
128. Yamaguchi-Shinozaki, K.; Shinozaki, K. Transcriptional regulatory networks in cellular responses and tolerance to dehydration and cold stresses. *Annu. Rev. Plant Biol.* **2006**, *57*, 781–803. [[CrossRef](#)] [[PubMed](#)]
129. Weigelt, K.; Küster, H.; Rutten, T.; Fait, A.; Fernie, A.R.; Miersch, O.; Wasternack, C.; Emery, R.J.N.; Desel, C.; Hoeslin, F.; *et al.* ADP-glucose pyrophosphorylase-deficient pea embryos reveal specific transcriptional and metabolic changes of carbon-nitrogen metabolism and stress responses. *Plant Physiol.* **2009**, *149*, 395–411. [[CrossRef](#)] [[PubMed](#)]
130. Bennett, R.N.; Wallsgrove, R.M. Secondary metabolites in plant defence mechanisms. *New Phytol.* **1994**, *127*, 617–633. [[CrossRef](#)]
131. Bachereau, F.; Marigo, G.; Asta, J. Effect of solar radiation (UV and visible) at high altitude on CAM-cycling and phenolic compound biosynthesis in *Sedum album*. *Physiol. Plant.* **1998**, *104*, 203–210. [[CrossRef](#)]
132. Cooper-Driver, G.A.; Bhattacharya, M. Role of phenolics in plant evolution. *Phytochemistry* **1998**, *49*, 1165–1174.
133. Kidd, P.S.; Llugany, M.; Poschenrieder, C.; Günsé, B.; Barcelò, J. The role of root exudates in aluminium resistance and silicon-induced amelioration of aluminium toxicity in three variety of maize (*Zea mays* L.). *J. Exp. Bot.* **2001**, *52*, 1339–1352. [[CrossRef](#)] [[PubMed](#)]
134. Stewart, A.J.; Chapman, W.; Jenkins, G.I.; Graham, I.; Martin, T.; Crozier, A. The effect of nitrogen and phosphorus deficiency on flavonol accumulation in plant tissues. *Plant Cell Environ.* **2001**, *24*, 1189–1197. [[CrossRef](#)]
135. Casati, P.; Walbot, V. Gene expression profiling in response to ultraviolet radiation in *Zea mays* genotypes with varying flavonoid content. *Plant Physiol.* **2003**, *132*, 1739–1754. [[CrossRef](#)] [[PubMed](#)]
136. Treutter, D. Significance of flavonoids in plant resistance and enhancement of their biosynthesis. *Plant Biol.* **2005**, *7*, 581–591. [[CrossRef](#)] [[PubMed](#)]
137. Treutter, D. Significance of flavonoids in plant resistance: A review. *Environ. Chem. Lett.* **2006**, *4*, 147–157. [[CrossRef](#)]
138. Caldwell, M.M.; Bornman, J.F.; Ballaré, C.L.; Flint, S.D.; Kulandaivelu, G. Terrestrial ecosystems, increased solar ultraviolet radiation, and interactions with other climate change factors. *Photochem. Photobiol. Sci.* **2007**, *6*, 252–266. [[CrossRef](#)] [[PubMed](#)]
139. Olsen, K.M.; Lea, U.S.; Sliemstad, R.; Verheul, M.; Lillo, C. Differential expression of the four *Arabidopsis* PAL genes –PAL1 and PAL2 have functional specialization in abiotic environmental triggered flavonoid synthesis. *J. Plant Physiol.* **2008**, *165*, 1491–1499. [[CrossRef](#)] [[PubMed](#)]
140. Adams-Phillip, L.; Briggs, A.G.; Bent, A.F. Disruption of poly(ADP-ribosyl)ation mechanisms alters responses of *Arabidopsis* to biotic stress. *Plant Physiol.* **2010**, *152*, 267–280. [[CrossRef](#)] [[PubMed](#)]

141. Fischer, R.S.; Bonner, C.A.; Theodorou, M.E.; Paxton, W.C.; Hrazdina, G.; Jensen, R.A. Response of aromatic pathway enzymes of plant suspension cells to phosphate limitation. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 1415–1420.
142. Van der Plas, L.H.W.; Eijkelboom, C.; Hagendoorn, M.J.M. Relation between primary and secondary metabolism in plant cell suspensions. *Plant Cell Tiss. Org.* **1995**, *43*, 111–116. [[CrossRef](#)]
143. Brown, J.K.M. Yield penalties of disease resistance in crops. *Curr. Opin. Plant Biol.* **2002**, *5*, 339–344. [[CrossRef](#)]
144. Messina, F.J.; Durham, S.L.; Richards, J.H.; McArthur, E.D. Trade-off between plant growth and defense? A comparison of sagebrush populations. *Oecologia* **2002**, *131*, 43–51. [[CrossRef](#)]
145. Cipollini, D.; Purrington, C.B.; Bergelson, J. Costs of induced responses in plants. *Basic Appl. Ecol.* **2003**, *4*, 79–85. [[CrossRef](#)]
146. Walters, D.; Heil, M. Costs and trade-offs associated with induced resistance *Physiol. Mol. Plant Pathol.* **2007**, *71*, 3–17. [[CrossRef](#)]
147. Ramakrishna, A.; Ravishankar, G.A. Influence of abiotic stress signals on secondary metabolites in plants. *Plant Signal. Behav.* **2011**, *6*, 1720–1731. [[PubMed](#)]
148. Vos, I.A.; Pieterse, C.M.J.; van Wees, S.C.M. Costs and benefits of hormone-regulated plant defences. *Plant Pathol.* **2013**, *62*, 43–55. [[CrossRef](#)]
149. Shetty, K. Role of proline-linked pentose phosphate pathway in biosynthesis of plant phenolics for functional food and environmental applications: A review. *Proc. Biochem.* **2004**, *9*, 789–803. [[CrossRef](#)]
150. Kushad, M.M.; Yelenosky, G. Evaluation of polyamine and proline levels during low temperature acclimation of citrus. *Plant Physiol.* **1987**, *84*, 692–695. [[CrossRef](#)] [[PubMed](#)]
151. Hare, P.D.; Cress, W.A. Metabolic implications of stress-induced proline accumulation in plants. *Plant Growth Regul.* **1997**, *21*, 79–102. [[CrossRef](#)]
152. Mehta, S.K.; Gaur, J.P. Heavy-metal-induced proline accumulation and its role in ameliorating metal toxicity in *Chlorella vulgaris*. *New Phytol.* **1999**, *143*, 253–259. [[CrossRef](#)]
153. Fedin, I.S.; Grigorova, I.D.; Georgieva, K.M. Response of barley seedlings to UV-B radiation as affected by NaCl. *J. Plant Physiol.* **2003**, *160*, 205–208. [[CrossRef](#)] [[PubMed](#)]
154. Kiyosue, T.; Yoshiba, Y.; Yamaguchi-Shinozaki, K.; Shinozaki, K. A nuclear gene encoding mitochondrial proline dehydrogenase, an enzyme involved in proline metabolism, is upregulated by proline but downregulated by dehydration in *Arabidopsis*. *Plant Cell* **1996**, *8*, 1323–1335. [[CrossRef](#)] [[PubMed](#)]
155. Hare, P.D.; Cress, W.A.; van Staden, J. Dissecting the roles of osmolyte accumulation in plants. *Plant Cell Environ.* **1998**, *21*, 535–553. [[CrossRef](#)]
156. Kavi Kishor, P.B.; Sangam, S.; Amrutha, R.N.; Sri Laxmi, P.; Naidu, K.R.; Rao, K.R.S.S.; Sreenath, R.; Reddy, K.J.; Theriappan, P.; Sreenivasulu, N. Regulation of proline biosynthesis, degradation, uptake and transport in higher plants: Its implications in plant growth and abiotic stress tolerance. *Curr. Sci.* **2005**, *88*, 424–438.
157. Szabados, L.; Savaouré, A. Proline: A multifunctional amino acid. *Trends Plant Sci.* **2010**, *15*, 89–97. [[CrossRef](#)] [[PubMed](#)]
158. Facchini, P.J. Plant secondary metabolism: Out of the evolutionary abyss. *Trends Plant Sci.* **1999**, *4*, 382–384. [[CrossRef](#)]
159. Blokhina, O.; Virolainen, E.; Fagerstedt, K.V. Antioxidants, oxidative damage and oxygen deprivation stress: A review. *Ann. Bot.* **2003**, *91*, 179–194. [[CrossRef](#)] [[PubMed](#)]
160. Gould, K.S.; Lister, C. Flavonoid functions in plants. In *Flavonoids—Chemistry, Biochemistry and Applications*; Andersen, Ø.M., Markham, K.R., Eds.; CRC Taylor & Francis: Boca Raton, FL, USA, 2006; pp. 397–411.
161. Lattanzio, V.; Cardinali, A.; di Venere, D.; Linsalata, V.; Palmieri, S. Browning phenomena in stored artichoke (*Cynara scolymus* L.) heads: Enzymic or chemical reactions? *Food Chem.* **1994**, *50*, 1–7. [[CrossRef](#)]
162. Fahrendorf, T.; Ni, W.; Shorrosh, B.S.; Dixon, R.A. Stress responses in alfalfa (*Medicago sativa* L.) XIX. Transcriptional activation of oxidative pentose phosphate pathway genes at the onset of the isoflavonoid phytoalexin response. *Plant Mol. Biol.* **1995**, *28*, 885–900. [[CrossRef](#)] [[PubMed](#)]
163. Hare, P.D.; Cress, W.A.; van Staden, J. Proline synthesis and degradation: A model system for elucidating stress-related signal transduction. *J. Exp. Bot.* **1999**, *50*, 413–434. [[CrossRef](#)]
164. Stewart, C.R.; Bogges, S.F.; Aspinall, D.; Paleg, L.G. Inhibition of proline oxidation by water stress. *Plant Physiol.* **1977**, *59*, 930–932. [[CrossRef](#)] [[PubMed](#)]
165. Hagedorn, C.H.; Yeh, G.C.; Phang, J.M. Transfer of 1-pyrroline-5-carboxylate as oxidizing potential from hepatocytes to erythrocytes. *Biochem. J.* **1982**, *202*, 31–39. [[CrossRef](#)] [[PubMed](#)]



166. Maggio, A.; Bressan, R.A.; Hasegawa, P.M.; Locy, R.D. Moderately increased constitutive proline does not alter osmotic stress tolerance. *Physiol. Plant.* **1997**, *101*, 240–246. [[CrossRef](#)]
167. Fine, P.V.A.; Miller, Z.J.; Mesones, I.; Irazuzta, S.; Appel, H.M.; Stevens, M.H.H.; Sääksjärvi, I.; Schultz, J.C.; Coley, P.D. The growth-defense trade-off and habitat specialization by plants in Amazonian forests. *Ecology* **2006**, *87*, S150–S162. [[CrossRef](#)]
168. Ncube, B.; Finnie, J.F.; van Staden, J. Dissecting the stress metabolic alterations *in vitro* *Cyrtanthus* regenerants. *Plant Physiol. Biochem.* **2013**, *65*, 102–110. [[CrossRef](#)] [[PubMed](#)]
169. Naliwajski, M.R.; Skłodowska, M. Proline and its metabolism enzymes in cucumber cell cultures during acclimation to salinity. *Protoplasma* **2014**, *251*, 201–209. [[CrossRef](#)] [[PubMed](#)]
170. Matyssek, R.; Agerer, R.; Ernst, D.; Munch, J.C.; Osswald, W.; Pretzch, H.; Priesack, E.; Schnyder, H.; Treutter, D. The plant's capacity in regulating resource demand. *Plant Biol.* **2005**, *7*, 560–580. [[CrossRef](#)] [[PubMed](#)]
171. Schloter, M.; Matyssek, R. Tuning growth *versus* defence–belowground interactions and plant resource allocation. *Plant Soil* **2009**, *323*, 1–5. [[CrossRef](#)]
172. Margna, U. Control at the level of substrate supply. An alternative in the regulation of phenylpropanoid accumulation in plant cells. *Phytochemistry* **1977**, *16*, 419–426. [[CrossRef](#)]
173. Margna, U.; Vainjärv, T.; Laanest, L. Different L-phenylalanine pools available for the biosynthesis of phenolics in buckwheat seedling tissues. *Phytochemistry* **1989**, *28*, 469–475. [[CrossRef](#)]
174. Jones, C.G.; Hartley, S.E. A protein competition model of phenolic allocation. *Oikos* **1999**, *86*, 27–44. [[CrossRef](#)]
175. Donaldson, J.R.; Kruger, E.L.; Lindroth, R.L. Competition- and resource-mediated tradeoffs between growth and defensive chemistry in trembling aspen (*Populus tremuloides*). *New Phytol.* **2006**, *169*, 561–570. [[CrossRef](#)] [[PubMed](#)]
176. Jiang, C.; Gao, X.; Liao, L.; Harberd, N.P.; Fu, X. Phosphate starvation root architecture and anthocyanin accumulation responses are modulated by the gibberellin-DELLA signaling pathway in *Arabidopsis*. *Plant Physiol.* **2007**, *145*, 1460–1470. [[CrossRef](#)] [[PubMed](#)]
177. Le Bot, J.; Benard, C.; Robin, C.; Bourgaud, F.; Adamowicz, S. The “trade-off” between synthesis of primary and secondary compounds in young tomato leaves is altered by nitrate nutrition: Experimental evidence and model consistency. *J. Exp. Bot.* **2009**, *60*, 4301–4314. [[CrossRef](#)] [[PubMed](#)]
178. Endara, M.-J.; Coley, P.D. The resource availability hypothesis revisited: A meta-analysis. *Funct. Ecol.* **2011**, *25*, 389–398. [[CrossRef](#)]
179. Arnholdt-Schmitt, B. Stress-induced cell reprogramming. A role for global genome regulation? *Plant Physiol.* **2004**, *136*, 2579–2586. [[CrossRef](#)] [[PubMed](#)]
180. Smirnoff, N. The role of active oxygen in the response of plants to water deficit and desiccation. *New Phytol.* **1993**, *125*, 27–58. [[CrossRef](#)]
181. Nanda, A.K.; Andrio, E.; Marino, D.; Pauly, N.; Dunand, C. Reactive oxygen species during plant-microorganism early interactions. *J. Integr. Plant Biol.* **2010**, *52*, 195–204. [[CrossRef](#)] [[PubMed](#)]
182. Razal, R.A.; Ellis, S.; Singh, S.; Lewis, N.G.; Towers, G.H.N. Nitrogen recycling in phenylpropanoid metabolism. *Phytochemistry* **1996**, *41*, 31–35. [[CrossRef](#)]
183. Van Heerden, P.S.; Towers, G.H.N.; Lewis, N.G. Nitrogen metabolism in lignifying *Pinus taeda* cell cultures. *J. Biol. Chem.* **1996**, *271*, 12350–12355. [[CrossRef](#)] [[PubMed](#)]
184. Mckey, D.; Waterman, P.G.; Mbi, C.N.; Gartlan, J.S.; Struhsaker, T.T. Phenolic content of vegetation in two African rain forests: Ecological implications. *Science* **1978**, *202*, 61–64.



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