| Publikacja / Publication | Biosynthesis Regulation of Folates and Phenols in Plants, Kołton Anna, Długosz-Grochowska Olga, Wojciechowska Renata, Czaja Monika |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| DOI wersji wydawcy / Published version DOI | http://dx.doi.org/10.1016/j.scienta.2021.110561 |
| Adres publikacji w Repozytorium URL / Publication address in Repository | https://repo.ur.krakow.pl/info/article/UR01e6911f740742cca71bf0ba8824704b/ |
| Data opublikowania w Repozytorium / Deposited in Repository on | Sep 14, 2021 |
| Rodzaj licencji / Type of licence | Attribution (CC BY) |
| Cytuj tę wersję / Cite this version | Kołton Anna, Długosz-Grochowska Olga, Wojciechowska Renata, Czaja Monika: Biosynthesis Regulation of Folates and Phenols in Plants, Scientia Horticulturae, vol. 291, 2022, pp. 1-15, DOI:10.1016/j.scienta.2021.110561 |
Review

Biosynthesis Regulation of Folates and Phenols in Plants

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ARTICLE INFO

Keywords:
Flavonoids
Folic acid
Photo regulation
Polyphenolic
Secondary metabolites

ABSTRACT

The latest knowledge regarding biosynthesis of folates and polyphenols is summarized, including factors modulating their accumulation in plants, with particular emphasis on light quality and quantity. Folates, essential elements in one-carbon metabolism, are required for several reactions important for the regulation of gene and protein expression, as well as lipid, chlorophyll, and lignin biosynthesis. Phenolic compounds play a pivotal role in the responses to certain stress conditions and function as reactive species scavengers, contributing to the maintenance of redox homeostasis in cells. These compounds are also essential for humans, and they are optimally absorbed via the consumption of plant-based foods. Light is a source of energy that triggers the light-phase reactions of photosynthesis in plants, but it also regulates the synthesis and accumulation of many metabolites, including folates and polyphenolic compounds, which are important for normal function. The use of adequate light conditions during the production of fruits and vegetables may contribute to an increase in the biological value of crops consumed as food. The potential role of artificial light in enhancing the folate and polyphenol content of food crops during cultivation and future perspectives of its use are also discussed.

1. Introduction

Plants are an important part of the human diet. An increased proportion of plants in the diet can support human health and contribute to the prevention of many diseases (Liu, 2013). Plant-based food introduces to the human diet a range of health-promoting compounds (phenolics, flavonoids, carotenoids, vitamin C, folates, minerals, fibre, chlorophylls, alkaloids, nitrogen-containing compounds, organosulfur compounds, phytosterols). The edible parts of plants can be fruits, leaves, roots, stems, flowers, seeds, cotyledons.

Folates are an essential part of a balanced human diet. Deficiencies of these compounds lead to many diseases such as megaloblastic anaemia, cognitive dysfunction, neurological and cardiovascular diseases, and different types of cancer (Ebara, 2017). Polyphenols are a group of bioactive compounds with a wide range of positive health effects (Wismuwardani et al., 2019). Their higher proportion in the diet is related to a lower risk of hypertension, type 2 diabetes, and cancer. There is also evidence that they can prevent obesity, cardiovascular and neurodegenerative diseases (Cory et al., 2018). Due to the wide spectrum of health benefits, an increased share of these compounds in plant production is desirable.

The chemical composition of plants changes very dynamically. Plants produce thousands of secondary metabolites that are distinguished from primary metabolites, such as sugars, amino acids, nucleic acids, and lipids (Kabera et al., 2014). Secondary metabolites are synthesized in plants in response to a specific need. It is worth emphasizing that the primary metabolism is the source of substrates for the production of secondary metabolites (Figure 1). Plant secondary compounds are often used by humans as medicines, flavourings, aromatic oils, dietary supplements, etc.

The primary and secondary metabolism depend on glucose concentration in plant tissue. Therefore, light plays a fundamental role in both metabolisms. Light not only provides the energy for glucose production in the photosynthesis process but also carries precise information indispensable for the recognition of changes in the environment. Specific pigments or protein-pigment complexes (photoreceptors) enable plants to receive and react to various wavelengths and portions of photons. Over the last decade, the knowledge regarding plant photoreceptors has expanded greatly (Galvão and Fankhauser, 2015; Paik and Huq, 2019; Teixeira, 2020). Plant photoreceptors are sensitive to
radiation from UV to far-red and regulate changes in morphology, physiology and metabolism. This makes plants very flexible in their ability to adjust to various spectral/light conditions.

Stage of development, soil type and nutrient availability, temperature, chemical elicitors, water supply, contamination, temperature and light are some of the factors regulating metabolite biosynthesis (Li et al., 2020). In our review, we describe briefly the chemical structures of folates and phenols and highlight their roles in the functioning of plant and human organisms. In the next section, we discuss in detail different factors influencing the biosynthesis of the compounds in question. We put special emphasis on the impact of light, as in the last years it has been investigated more and more in response to the growing popularity of LED lamps. Finally, we consider directions for future research.

Fig. 1. The connection between the primary and secondary metabolism in plants - selected elements.
2. Folates

The basic structure of the folate comprises three residues: a pteridine ring, p-aminobenzoate, and glutamate. Folate diversity is due to different degrees of oxidation, the variety among added one-carbon (1C) groups, the length of the polyglutamyl chain, and the possibility of creating adducts with other molecules, such as sugars or proteins. Folates are water-soluble vitamins and, depending on the form, are pale to dark yellow. Folates are labile compounds with particular sensitivity to high temperatures and intense light, especially UV (Juzeniene et al., 2013). Moreover, they are claimed to play a role in redox homeostasis as they show anti-radical (Joshi et al., 2001) and antioxidant properties (Gliszczynska-Swiglo, 2006).

2.1. Chemical structure

The term ‘folates’ refers to a group of naturally occurring heterocyclic compounds, constituted by three moieties: 2-amino-4-hydroxy-pteridine, p-aminobenzoate, and mono- or poly-γ-glutamate (Blakley and Jude, 1987) (Figure 2). The 1C units that may be attached to the N5 and/or N10 of the folate molecule are methyl (CH$_3$-), methenyl (-CH$^+$-), methylene (-CH$_2$-), formyl (HCO-), and formimino (NHCH-) groups (Blakley and Jude, 1987). Given the multitude of potential combinations of the attached 1C units, the oxidation of the pteridine ring, and the length of the polyglutamate chain, these compounds make up a group that comprises of about 150 distinct molecular species. The term folic acid (FA) is reserved for its synthetic form, with an oxidized pteridine ring and no attached 1C units. Folic acid is one of the most stable forms of vitamin B9 and is relatively inexpensive to produce, thus it is used for the production of commercially available pills offered as a dietary supplement.

![Structure of naturally occurring folates (tetrahydrofolate and its derivatives). R1 and R2 represent one-carbon substituents shown in the table below the figure.](image)

| R1 (N5) | R2 (N10) | NAME |
|---------|---------|------|
| - H     | - H     | tetrahydrofolate (THF) |
| - CH    | - H     | 5 - methyl - tetrahydrofolate |
| - CHO   | - H     | 5 - formyl - tetrahydrofolate |
| - CHNH  | - H     | 5 - formimino- tetrahydrofolate |
| - H     | - CHO   | 10 - formyl - tetrahydrofolate |
| - H     | - CHNH  | 10 - formimino- tetrahydrofolate |
| - CH$_2$ (bridge) | 5,10 - methylene - tetrahydrofolate |
| - CH$^+$ (bridge) | 5,10 - methenyl - tetrahydrofolate |
2.2. Function in living organisms and importance for human health

Folates are a very important group of compounds that are necessary for the proper functioning of every living organism. They have been classified as water-soluble vitamin B9, included in the B-complex vitamins (Ferrazzi et al., 2020). They are a focal point of 1C metabolism in cells (Hanson and Gregory, 2011), serving as a 1C carrier, taking a 1C unit from a donor (e.g. serine) and transferring it to an acceptor (Zheng and Cantley, 2019). Many physiological processes, e.g.: purine and thymidine monophosphate biosynthesis, methionine regeneration, and mitochondrial protein translation (Zheng and Cantley, 2019), require folates for the 1C unit transfer. As suppliers of methyl groups, folates are necessary for methylation reactions, which are not only important for the regulation of gene expression, but also involved in the biosynthesis of proteins, lipids, chlorophyll, and lignin. The efficient functioning of the reactions listed above determines further key processes in cells, such as epigenetic regulation, cell proliferation, and mitochondrial respiration (Zheng and Cantley, 2019), as well as photosynthesis in plants (Gorelova et al., 2017). All these reactions are crucial for maintaining the healthy functioning of an organism. However, animals (including humans) lack de novo biosynthetic pathways for folates, thus suitable amounts of these compounds must be provided through food intake. Insufficient dietary uptake of FA derivatives has been linked to the occurrence of anaemia and increased risk of developing diseases of the cardiovascular and nervous systems, as well as the development of neural tube defects in the foetus (Delchier et al., 2013). Low concentrations of plasma folate in humans are also linked to certain types of cancer (Blancquaert et al., 2010), depression, and other mental disorders (Abou-Saleh and Coppen, 2006). Recent studies have also shown a connection between low levels of blood folate plasma and obesity (Köse et al., 2020).

Dietary supplements and products artificially fortified with FA are commonly used to prevent folate deficiency, especially at critical stages of life when their presence is crucial for the proper development and functioning of the body (e.g. during the development of the nervous system in the human foetus) (Valentin et al., 2018; Viswanathan et al., 2017). The World Health Organization recommends an adult daily uptake of folate of 400 µg, increased to 600 µg during pregnancy (FAO/WHO, 2020). However, highly-stable FA produced synthetically, used to fortify foods and supplements, is inactive in the human body and must be transformed to active 5-MTHF (5-methyl-tetrahydrofolic acid) by hepatic reductases in the liver (Ferrazzi et al., 2020; Wusigale and Liang, 2020). In certain conditions, the hepatic enzymes are not able to perform FA reduction (e.g. megaloblastic anaemia or excessive FA supplementation), which may result in the concentration of this compound in the blood becoming too high, despite symptoms of deficiency of the active form of folate (Ferrazzi et al., 2020). The problem of unmetabolized FA circulating in the bloodstream has recently attracted the attention of researchers as it may contribute to adverse reactions. For example, children with high levels of unmetabolized FA in their blood tend to develop food allergies and intolerances (McGowan et al., 2020). Due to the issues mentioned above, recent studies have focused on the form in which folates are consumed. An effective way to prevent folate deficiency is to consume folates in their natural form, which is found in significant amounts in many plant-based foods. In general, vegetables are thought to be richer in folates than fruits, however, the concentration of these compounds is highly dependent on species, cultivar, climate, and manner of cultivation, so wide variations are visible within the same vegetable. Among vegetables, high folates content can be found in spinach (Spinacia oleracea L.; a mean of 165 µg/100 g f.w.), green peas (Pisum sativum L.; up to 156 µg/100 g f.w.), turnips (Brassica rapa var. rapa L.; around 124 µg/100 g f.w.), and broccoli (Brassica oleracea var. italica L.; up to 100 µg/100 g f.w.) (Delchier et al., 2016). Amongst fruits, the richest in folates are muskmelon (Cucumis melo L.; a mean of 115 µg/100 g f.w.), strawberries (Fragaria × ananassa Duchesne; around 47 µg/100 g f.w.), and kiwi (Actinidia sp. Lindl.; 42 µg/100 g f.w.) (Delchier et al., 2016). Thus, taking into account all the factors mentioned above, research on the natural methods of folates accumulation in crop plants (e.g. temperature, light conditions, or fertilization) is clearly needed.

2.3. Biosynthesis of folates in plants

Among living organisms, only plants, fungi, and bacteria have the ability to synthesize folates de novo. The individual steps of plant folates biosynthesis have been well described and are assumed to be quite conserved amongst organisms. The process starts in the cytosol, where pterine is synthesized from guanosine triphosphate (GTP) (Figure 3).

The first reaction in this pathway, the conversion of GTP into dihydrofolate phosphorylase and formate, catalysed by GTP cyclohydrolase I (GTPCHI), is a key stage that determines the efficiency of the whole process of folate biosynthesis (Hossain et al., 2004). The next steps include the dephosphorylation and removal of the lateral side chain from the dihydrofolate molecule, resulting in the formation of 6-hydroxymethyl-7,8-dihydropteridine (HMDHP) (Gorelova et al., 2017). The second component of folate, pABA (para-aminobenzoic acid), is synthesized from chorismate. The reactions occur in the plastids and start with the conversion of chorismate and glutamine to aminodeoxychorismate and glutamate by aminodeoxychorismate synthase (ADCS). Next, aminodeoxychorismate lyase (ADCL) converts aminodeoxychorismate into pABA. Subsequently, pABA may be used in folate synthesis or converted by the action of uridine diphosphate (UDP)-glucosyltransferase to its glucose ester for storage (Gorelova et al., 2017). Both ADCS and ADCL were found to be inhibited by high concentrations of pABA, pABA glucose ester, and some forms of folate (Basset et al., 2002; 2004). HMDHP is transported to the mitochondria, where pyrophosphorylation, catalysed by HMDHP pyrophosphokinase (HPPK), occurs. After that, the enzyme dihydropterate synthase (DHPS) contributes to the combination of pABA and HMDHP-P2, resulting in the formation of dihydropterate (DHP). Connecting the glutamate moiety to DHP via dihydrofolate synthase (DFHS) and reducing the molecule to form tetrahydrofolate (THF) via dihydrofolate reductase (DHFR) completes the biosynthetic pathway of tetrahydrofolate, which may be transported to different subcellular structures or connected to more glutamate residues in reactions catalysed by folylpolyglutamate synthase (FPGS) (Gorelova et al., 2017).

2.4. Regulation of folates biosynthesis in plants

2.4.1. Control points within folates biosynthesis pathway

As mentioned above, folates act as an extremely important cofactor in numerous crucial physiological reactions. Thus, matching folates production levels with current demand is very important for maintaining the smooth functioning of metabolic pathways. Although the regulation of folates biosynthetic enzyme activity is still not fully understood, certain points in the biosynthetic pathway that are regulated in response to the concentration of intermediate metabolites have been identified. The first of these is the enzyme DHPS. Its activity is controlled by the reaction product dihydropterate, which competes with two reaction substrates, pABA and 6-hydroxymethyl-7,8-dihydropteridine pyrophosphate (Rebeille et al., 1997). Since THF stands at the centre of 1C reactions, it has been hypothesized that the products of 1C metabolism may also play a regulatory role in controlling enzymes in the folate biosynthetic pathway (Scott et al., 2000). However, the support for this hypothesis relies only on research conducted on fungi, where the activities of the enzymes involved in folates biosynthesis are controlled by methionine and homocysteine, the former acts as a repressor and the latter as an inducer of the FPGS and DHFR enzymes (Lewandowska et al., 1996).

2.4.2. Chemical elicitors

In order to improve the quality of crop plants by enhancing folates...
concentrations, some attempts have been made to use chemical elicitors. For example, treating coriander plants with salicylic acid resulted in a doubling of the total folates concentration in the leaves, as well as a 10% improvement in the stability of folates in this plant (Puthusseri et al., 2012, 2013). Also, treatment of spinach with phenylalanine caused a two-fold increase in folates concentration by activating the synthesis of pteridine and pABA (Watanabe et al., 2017).

2.4.3. Folates response to stage of plant development

Folates are very important during the development of tissues and organs. Since they play a crucial role as a cofactor during DNA and protein synthesis and maturation, high concentrations of folates are needed physiologically for normal tissue and organ growth and development. Thus, the age of plants and organs would be a factor that forces high levels of folates synthesis. High levels of expression of the genes involved in folates synthesis have been found in rapidly dividing tissues - meristems of carrot (Daucus carota L.) (Albani et al., 2005), pea (Pisum sativum L.) (Jabrin et al., 2003), and maize (Zea mays L.) (Cox et al., 1999). Further, high expression levels of folates-related genes with simultaneous high concentrations of these compounds occur in plant embryos (Jabrin et al., 2003; Gambonnet et al., 2001). Moreover, mutants defective in folates biosynthesis have been found to be embryo-lethal (Ishikawa et al., 2003; Mehrshahi et al., 2010), which suggests these compounds perform a crucial and irreplaceable function in developmental processes. It seems that during development folates concentrations are higher in younger organs than in older ones, supporting a connection between low folates levels and plant senescence. Abnormal folates metabolism may contribute to altered H₂O₂ production, which causes early senescence symptoms in the leaves of rice (Oryza sativa L.) (Xiong et al., 2020). The influence of the supply of exogenous folates on the post-harvest ageing of broccoli (B. oleracea var. italica L.) has also been investigated. Research shows that treating broccoli heads with an FA solution, among others, inhibited the opening of flower buds and the degradation of chlorophyll, limited the production of ROS, and slowed down the ageing processes in tissues (Xu et al., 2020).

2.4.4. Soil type and nutrients

Soil is the main source of macro- and micronutrients necessary for the growth and development of plants. Therefore, the abundance of nutrients in the soil and their availability to plants in many cases determine the functioning of metabolism, including the biosynthesis of plant secondary metabolites. For example, a two-fold increase in folates concentration was found by Lester and Crosby (2002) in melons (C. melo L.) grown in clay-loam soil compared to sand-loam soil. More specific research conducted by Mozafar (1994) indicated that vitamin B-complex content, in which folates are present, tends to increase when the plant has better access to elements such as nitrogen, phosphorus, and boron. Moreover, the literature supports the hypothesis that organic fertilization has a positive effect on the synthesis of B vitamins, including FA derivatives. For instance, Lester (2006) observed that the use of organic manure instead of mineral fertilizers increased the concentration of folates in plants.

Fig. 3. Folates biosynthesis in plants with steps indicated where light regulation may occur. Precursors and products are shown in brown. The enzymes involved in various stages of the biosynthesis are shown in blue. The dashed line indicates more than one reaction. Abbreviations: GTP – guanosine triphosphate; DHN-P₃ – dihydroneopterin triphosphate; DHN-P – dihydroneopterin monophosphate; DHN – dihydroneopterin; HMDHP – 6-hydroxymethylidihydropterin; HMDH-P₂ – 6-hydroxymethylidihydropterin pyrophosphatase; DHF – dihydrofolate; THF – tetrahydrofolate; THF-Glu(n) – tetrahydrofolate polyglutamate; ADC – aminodeoxychorismate; pABA – para-aminobenzoic acid. Enzymes: GTPCHI – GTP cyclohydrolase I; DHNP3-diphosphatase – dihydroneopterin triphosphate pyrophosphatase; DHNA – dihydroneopterine aldolase; HPPK – HMDHP pyrophosphokinase; DHPS – dihydropteroate synthase; DHFR – dihydrofolate reductase; FPGS – folylpolyglutamate synthase; ADCS – aminodeoxychorismate synthase; ADCL – aminodeoxychorismate lyase; GGH – gamma-glutamyl hydrolase. Adapted and modified after Gorelova et al. (2017).
many vitamins, including vitamin B-complex, in carrots (D. carota L.). Conversely, in the research of Kongkachuichai et al. (2019) on 10 species of fruits and vegetables grown in Thailand, including kale (B. oleracea L.), cabbage (B. oleracea var. capitata L.), and carrots, no significant differences were found in folates concentration between the organic and inorganic mode of cultivation. On the other hand, the studies of Meng et al. (2014, 2017) involving Arabidopsis thaliana-3 mutants deficient in FPGS showed that this enzyme is vital to the normal regulatory functions of nitrate metabolism under nitrate-limited conditions in darkness, which indicates the significance of folates polyglutamylation for plant nitrogen metabolism in light-deficient conditions.

2.4.5. Temperature

Temperature is a general climatic factor that affects the growth and development of all species, including secondary metabolite synthesis. However, little attention has been paid to the impact of temperature regimes on folates biosynthesis and accumulation in fresh plants. Recently, novel research has been published on the effect of temperature during lettuce (Lactuca sativa L.) cultivation on leaf folates content. In the study of Okazaki and Yamashita (2019) even though the physiological temperature optimum of lettuce is approximately 20 °C, the highest folates content was found in plants grown at slightly higher than optimal temperature conditions, namely 25 °C. However, a higher temperature (28 °C) caused a significant decrease in the content of folates, suggesting that high temperatures negatively influence folates biosynthesis in lettuce (Okazaki and Yamashita, 2019). More attention has been paid to the influence of temperature on the folates content of harvested fruits and vegetables, as this is an important issue for maintaining the shelf life of plant foods during transport and display. For example, O’Hare et al. (2012) studied choy sum leafy vegetable (B. rapa var. parachinensis L. H. Bailey) stored for three weeks at a low temperature (4 °C) and showed unchanged levels of total folates in edible tissues, while folates storage reserve was interconverted to metabolically active 5-MTHF (O’Hare et al., 2012). In general, the storage of fresh plant foods at low temperatures (4 °C) causes a slower loss of folates than storage at room temperature, but the rate of degradation of these compounds is dependent on the species and variety of the stored plant (Díaz de la Garza et al., 2019).

2.4.6. Light

As mentioned in the Introduction, light is an important environmental factor that affects almost all the processes of a plant organism. However, in terms of the influence of light on folates biosynthesis, published results are not consistent and further comprehensive studies are needed to obtain a complete picture of how folates biosynthesis responds to light stimuli. For example, studies on mustard greens (Brassica juncea L. Czern.) showed no particular effect of light stimuli on the folates content of leaves in light- and shade-grown plants (Makus and Lester, 2002). But the inseparable link between folates-mediated 1C metabolism and photosynthesis suggests the existence of a relationship between light intensity and the reactions that occur during folates biosynthesis (Okazaki and Yamashita, 2019; Hanson and Roje, 2001).

Support for this hypothesis may be provided by recent research on lettuce, in which plants grown under a higher photosynthetic photon flux density (PFD = 200 μmol m⁻² s⁻¹) had higher concentrations of folates in comparison to plants grown under lower light intensity (PFD = 150 μmol m⁻² s⁻¹) (Okazaki and Yamashita, 2019). The same study showed that it is not only PPDF that is important for folates biosynthesis levels, but also that the spectral composition of light contributes to the higher expression of these compounds. Specifically, an addition of green (G) light to the red (R) and blue (B) wavelengths caused an increase in folates production in cultivated lettuce, compared to a situation when only R and B light were present (Okazaki and Yamashita, 2019). Similarly, studies of Długoż-Grochowska et al. (2016) on lamb’s lettuce (Valerianella locusta L.) grown in a greenhouse with LED supplemental lighting showed that supplementing red and blue light with bands corresponding to intermediate colours (green and yellow) through the use of cool and warm white light contributed to higher concentrations of folates in the leaves of this vegetable than in the case when red-blue light, red light only, or sodium lamps (with reduced emission of red wavelengths) were used. Equally high levels of FA derivatives were achieved by using an appropriate proportion of red and blue light, especially in the ratios of 9:1 and 7:3 (Długoż-Grochowska et al., 2016). However, other research conducted on lettuce, which aimed to compare different LED light spectra, indicated that an addition of white LED light to the red and blue spectrum did not result in a higher folates concentration in leaves. The use of red and blue diodes in the proportion of 4:1 (red to blue wavelengths) contributed to the highest folates content in illuminated plants (Hytonen et al., 2017). Other studies supporting the hypothesis that light affects folates biosynthesis in plants were conducted by Gambernet et al. (2001) using pea (P. sativum L.) seedlings, and folates concentrations recorded in green leaves were higher than in etiolated ones (Gambernet et al., 2001). Further studies of Jabrin et al. (2003) showed that during the first 8 h of pea seedling de-etiolation folates concentration remains low, but it then starts to increase slowly and after 24 h of light exposure reaches levels similar to those of plants grown under constant light conditions. Furthermore, in pea seedlings undergoing de-etiolation, a gradual light-induced increase in the expression of the gene encoding the HPPK/DHPS enzyme was found, which is strong evidence of the involvement of light in folates synthesis in young and developing plants (Jabrin et al., 2003).

Chorismate is a precursor of the pABA moiety of folates. It is synthesized from phosphoenolpyruvate and erythrose 4-phosphate in the so-called shikimate pathway, involving several enzymes. Two of them have been found to be activated in light conditions: 3-deoxy-a-arabino-heptulosonate 7-phosphate synthase (DAHPS) (Henstrand et al., 1992) and 3-Dehydroquinase/Shikimate dehydrogenase (DHQ/SDH) (Weaver and Herrmann, 1997). Light-induced accumulation of chorismate may indirectly affect the efficiency of folates production. In studies of the very early stages of a plant’s life, a peak of folates concentration was observed when maize (Z. mays L.) was sprouting under light conditions whereas no peak in folates concentration was found in maize sprouting in the dark, which suggests that light stimuli have a potential regulatory influence on folates biosynthesis (Liu et al., 2017). Lester et al. (2010) carried out research regarding the influence of postharvest storage conditions on maintaining a high level of folates in plant tissues and found that constant light combined with low temperature (4 °C) results in an increase in folates concentration during postharvest storage of spinach leaves (S. oleracea L.) (Lester et al., 2010). The steps in folates synthesis that may be affected by light stimuli were indicated in Figure 2.

Although the results of research on the influence of light on folates synthesis in plants are not consistent, there are some obvious conclusions connecting light stimuli and the production of these compounds. The great diversity of species-specific responses should also be taken into account. Therefore, more specific molecular studies involving gene expression, protein levels, and activity on a broad range of different plant species are needed to obtain a full picture of the influence of light on folates metabolism in plants. At the same time, this knowledge can be used in the production of high-quality plant products by using the appropriate intensity and spectral composition of light in greenhouses and growing rooms when fruits and vegetables are growing.

3. Phenolic compounds

Phenolic compounds are very diverse, from simple phenolic acids with one phenolic ring to polymers with very complex structures. Thousands of different phenolic compounds have been described in plants, and their number is constantly growing. Phenolic compounds can undergo glycosylation, acylation, or methylation, which changes their chemical properties and biological activity. Phenolic compounds have many interesting chemical properties. The free radicals formed...
from them are relatively long-lived and the free electron is delocalized. Some of them are very good antioxidants, they can be oxidized, they have the ability to chelate metal ions, and they also exhibit the properties of weak acids. The hydroxyl group of phenolic compounds is a good donor of hydrogen. Lower molecular weight phenols can be volatile and have an odour. Phenolic compounds range in colour from white to yellow and from red to blue and purple (Cheynier et al., 2015).

### 3.1. Chemical structures and classification

Phenolic compounds are a huge group of the secondary metabolites produced by plants, the common element of which is the aromatic ring connected to at least one hydroxyl group. Phenols comprise simple compounds with low molecular weights as well as very complex polymers with a masses above 20,000 Da (Bohn, 2014; Santana-Galvez and Jacobo-Velázquez, 2018; Durazzo et al., 2019). There are several ways to classify phenolic compounds, taking into account their chemical properties: number of aromatic rings, number of carbons in the skeleton, number of hydroxyl groups, solubility, etc. One method of classification is presented in Table 1 and Figure 4, based on the number of aromatic rings, followed by the carbon skeleton, and basic chemical structure (Santana-Galvez and Jacobo-Velázquez, 2018; Vermerris and Nicholson, 2008). A slightly different way of classifying phenolic compounds has been presented by Tsimogiannis and Oreopoulou (2019), but both systems are similar in many points.

### 3.2. Function in living organisms and importance for human health

There is a view that the ability to produce phenolic compounds that protect plant cells against UV radiation enabled plants to settle the terrestrial environment (Cheynier et al., 2013). Phenolic secondary metabolites fulfil many functions in plant organisms. They not only serve as a UV filter/screen, but also take part in interactions with the environment, provide a defence mechanism against biotic and abiotic stresses, cooperate with hormones (e.g. auxins), and give colour to plant organs. Phenolic compounds are widely distributed throughout the plant kingdom.

The role of phenolic compounds in the plant defense system is very interesting. Wild plants of Nicotiana attenuata Torr. ex S.Watson treated with radiation enriched with UVB produced more phenolic compounds (rutin, chlorogenic acid, caffeoyl putrescine, daicaffeyl spermidine) than plants treated with radiation without UV (Demkura et al., 2010). At the same time, treatment with UVB enriched radiation results in less pest damage to the leaves. Some plant defense responses are independent of light, but light has been shown to be essential during salicylic acid-dependent responses (Roden and Ingle, 2009). During a biotrophic pathogen infection the activation of defence mechanisms associated with salicylic acid (simple phenolic acid) is often related to growth inhibition (Albrecht and Argyuso, 2017). This phenomenon is described as the growth-defence trade-off. The role of phenolic compounds in the interaction between light and plant defense against pathogens and pests has been widely described by Roberts and Paul (2006) and Iqbal et al. (2021), but a thorough description of these phenomena is beyond the scope of this review. Increased synthesis of phenolic compounds in plants during greenhouse production with specific LED lamps may stimulate plant resistance to diseases and pests and contribute to the reduction of the use of plant protection chemicals (Lazzarini et al., 2021). Moreover, optimal light conditions promoting the synthesis and

#### Table 1

| Number of aromatic ring | Carbon skeleton | Group name | Subclass | Example |
|-------------------------|----------------|------------|----------|---------|
| One                     | C6             | Simple phenols | thymol, resorcinol, orcinol |
|                         | C6-C1          | Phenolic acids | gallic acid, salicylic acid, syringic acid, protocatechueic acid, p-hydroxybenzoic acid |
|                         |                | Phenolic aldehydes | vanillin, syringaldehyde, p-hydroxybenzaldehyde |
|                         | C6-C2          | Acetophenones | 2-hydroxyacetophenone |
|                         |                | Phenylactic acids | 2-hydroxyphenylacetic acid |
|                         | C6-C3          | Hydroxycinnamic acids | caffeic acid, cinnamic acid, p-coumaric acid, ferulic acid, sinapic acid, 5-hydroxyferulic acid, chlorogenic acid |
|                         |                | Coumarins | coumarins, isocoumarins |
|                         |                | Phenyl propenes | umbelliferone, aesculetin, scopoletin |
|                         |                | Chromones | |
|                         |                | Naphthoquinones | |
|                         | C6-C1-C6       | Xanthones | plumbagin, alkannin, lawson, juglone |
|                         | C6-C2-C2       | Stilbenes | resveratrol |
|                         |                | Anthraquinones | emodin, physcion, catearin, rhein |
|                         | C6-C3-C6       | Flavonoids | naringenin, taxifolin, leuodendphinidin, catechin, kaempferol, queretin, pelargonidin, cyanidin, delphinidin |
|                         |                | Isoflavonoids | genistein, daidzein, glycitein |
|                         |                | Neoflavonoids | |
|                         |                | others | |
|                         |                | Neolignans | chloridizin, aureusidin |
|                         |                | (C6-C3)2 | (-)-pinoresinol, (+)-sesamin, (-)-plicatic acid |
| Three or more           | (C6)n          | Catechol melanins | |
|                         | (C6-C3)n       | Lignins | amentoflavone, ochnaflavone, ginkgetin |
|                         | (C6-C3-C6)2    | Biflavonoids | |
|                         |                | 2 | |
|                         | (C6-C3-C6)n    | Condensed tannins | |
accumulation of phenolic compounds in tissues exposed to pathogens or pests contribute to increasing plant resistance to biotic stress factors and can lead to a reduction in tissue and organ damage. As a result, there is no need to redirect energy and metabolites to fight the attacking organism (what may cause disturbances in plant growth and development), and the resources can be used to build biomass. Proper growth and development is particularly important for crop plants, since the proper allocation of energy in the form of biomass of usable organs determines obtaining a profitable and high quality yield.

The structure of phenolic compounds is very diverse, so they perform a range of functions for humans. They can be food colourings or flavourings, and some are used as drugs or dietary supplements. Phenolic compounds are common in plants, including edible ones, and therefore are part of the human diet, in which they are also the main antioxidant.

Fig. 4. The structure of selected phenolic compounds with an example in each presented class and an indication of the structure of the carbon skeleton (in the lower left corner of each rectangle).
acids, including the shikimate pathway. The latter pathway produces aromatic amino phosphate from the pentose phosphate cycle produce shikimic acid via pathway. Phosphoenolpyruvate from glycolysis and erythrose-4-

development and progression of cancer (Niedzwiecki et al., 2016). Polyphenols in combination are effective in counteracting the development and progression of cancer (Niedzwiecki et al., 2016).

In general, epidemiological studies show a diet rich in polyphenols or phenolic acids positively inhibits the development of many diseases. However, in clinical trials, negative effects are often associated with the administration of isolated single phenolic compounds. The reason for this effect may be a change in the bioavailability of phenolic compounds or interaction with other dietary components (Bohn, 2014; Kumar and Goel, 2019). Phenolic compounds undergo many changes in the human digestive tract, which affect their chemical properties (Kawahata et al., 2019). An excess of ingested polyphenols may also have a potentially pro-oxidative effect, causing the formation of hydroxyl radicals in the Fenton reaction after the reduction of transition metal ions, such as iron. Some polyphenols can be oxidized to quinones and engage in redox cycles that produce free radicals. Most dietary polyphenols can chelate iron in the gut, increasing the risk of iron deficiency (Bohn, 2014; Scalbert et al., 2005). However, more clinical trials are needed to obtain a comprehensive view of the importance and potential hazards of consuming phenolic compounds concerning human health. To date, there are no recommendations for daily allowances of phenolic compounds, and research is ongoing (Williamson, 2017).

3.3. Biosynthesis of phenolic compounds in plants

It is easy to imagine that such a diverse group of compounds arises through many biosynthetic pathways. However, the source of the initial compounds in the synthetic pathways is, of course, primary metabolism: glycolysis, the formation of acetyl-CoA, and the pentose phosphate pathway. Phosphoenolpyruvate from glycolysis and erythrose-4-phosphate from the pentose phosphate cycle produce shikimic acid via the shikimate pathway. The latter pathway produces aromatic amino acids, including l-phenylalanine. This is where the phenylpropanoid pathway begins, resulting in p-coumaroyl CoA formation. This compound is used for the production of phenylpropanoids and monolignols, or, after condensation with three malonic acid molecules, forms more complex phenolic compounds such as stilbenes or flavonoids. Compounds from other pathways, such as the mevalonate pathway, can participate in the synthesis of some phenolics. A simplified synthesis scheme is shown in Figure 5, and the known pathways are described in the literature (Vermerris and Nicholson, 2008; Salzveis, 2016; Chaynier et al., 2013; Santana-Galvez and Jacobo-Velazquez, 2018).

3.4. Regulation of phenolic compound synthesis in plants

Phenolic compounds are produced in plants in response to external (environmental) or internal (developmental) factors. It follows that their synthesis is broadly regulated. We can consider the spatio-temporal expression of the genes involved in the synthesis, i.e. where (in what cells, tissues, or organs) the synthesis occurs and when (in what developmental phase). The genes encoding the enzymes involved in the synthesis (structural genes) or those that encode transcription factors (TFs) or repressors (regulatory genes) can be analysed. Regulatory gene products stimulate or inhibit the expression of structural genes in a response to factors (Vermerris and Nicholson, 2008). However, it is not always possible to determine the expression of the genes responsible for the synthesis and we, therefore, infer the regulation of biosynthesis based on the presence of an increased or decreased amount of a metabolite. Additionally, altered gene expression does not always translate into increased protein activity and metabolite production. Post-transcriptional or post-translational regulation can also occur. Thus, it is also important to determine the activity of the enzyme proteins involved in biosynthesis. Summing up, when examining the influence of factors on the regulation of a given synthesis pathway, the expression of the genes involved in the synthesis, the expression of the proteins resulting from such gene expression, the activity of these proteins, and the amount of the metabolite formed should all be considered (Stitt and Gibon, 2014).

Transcription factors regulate the expression of other genes by binding to DNA. In maize TFs that react with the promoters of a phenolic gene have been identified from seven different families (Yang et al., 2017). Among the key regulators of phenylpropanoid synthesis are MYB (V-myb myeloblastosis viral oncogene homolog) TFs (Liu et al., 2015). Many MYB TFs have been found to regulate the phenylpropanoid pathway in plants, some of them work as activators, others as repressors. Also, one MYB TF can regulate multiple genes in the pathway, and one gene can be regulated by multiple MYB proteins (see review: Liu et al., 2015). The TFs important in flavonoid synthesis are bHLH (basic helix-loop-helix), MYB, WD40, WRKY, Zinc finger, and MADS box proteins (Zhou et al., 2013).

3.4.1. Hormones

Some evidence exists that hormones regulate phenolics biosynthesis. For example, ethylene and (S)-cis-α-bisic acid (S-ABA) improve berry colour in grapes (Vitis vinifera L.). The colour is an effect of the accumulation of anthocyanins. Treatment of hybrid grapes (Vitis vinifera L. × V. labrusc aus L.) with S-ABA modulates anthocyanin regulatory and biosynthetic genes, as well as the accumulation of these pigments (Koyama et al., 2018).

3.4.2. Developmental phase

In plant cultivation, the questions often arise if and how the phenolic compound content is regulated during developmental phase changes. The changes in fruits associated with maturation are those that have been most extensively studied. Changes in the level of the expression of the proteins involved in the synthesis of phenolic compounds have been observed during blueberry (Vaccinium corymbosum L.) fruit maturation, along with corresponding changes in the phenolic compound content (Li et al., 2019). During the transition from the green to the blue phase of fruit maturation, downregulation of the proteins responsible for ferulic acid and catechin synthesis was observed, as well as a decrease in the content of these compounds. At the same time, upregulation of the proteins related to the production of quercetin, myricetin, and anthocyanins was noted. In sweet pepper fruits (Capsicum annuum L.) an accumulation of phenolic compounds during ripening has also been observed (Kolton et al., 2011). Red fruits contain significantly more phenolic compounds than fully-grown green ones. Development-dependent accumulation of phenolic compounds has been observed in tea plants (Camellia sinensis L.) (Jiang et al., 2013). Younger leaves were enriched in most phenolic compounds, although some molecules (such as proanthocyanidins) were specific to the roots or quinic acid the stem. Also, the expression of the genes related to phenolic biosynthesis was specific to the tissue and developmental phase. Likewise, in yarrow (Achillea millefolium L.) the expression of PAL and CHS is tissue- and phase-dependent, expression in flowers has been found to be higher than in leaves, and in the case of leaves increased expression has been observed in young leaves compared to fully expanded ones (Fathi et al., 2019). These examples are clear evidence that the synthesis of phenolic compounds is extensively regulated during changes in the developmental phases and ripening of fruit.
Fig. 5. A scheme of the synthesis of phenolic compounds in plants. The full names of precursors and main products are shown. The enzymes involved in individual steps of the biosynthesis are presented as abbreviations. Abbreviations: PAL - phenylalanine ammonia lyase, C4H - cinnamate-4-hydroxylase, 4CL - coumarate CoA ligase, STS - stilbene synthase, CHS - chalcone synthase, CHI - chalcone isomerase, FNS - flavone synthase, F3H - flavanone 3-hydroxylase, F3′H - flavonoid 3′ hydroxylase, F3′5′H - flavonoid 3′5′ hydroxylase, FLS - flavonol synthase. Adapted and modified after Cheynier et al. (2013), Winkel-Shirley (2001) and Jiang et al. (2013).
3.4.3. Water

Changes in the expression of the genes encoding enzymes in the phenylpropanoid pathway have been observed in basil (Ocimum basilicum L.) after a drought (Mandoulakani et al., 2017). The levels of activity of cinnamate 4-hydroxylase (C4H) and 4-coumarate CoA ligase (4CL) were reduced under drought stress. Similarly, Gharbi et al. (2019) observed an increase in the content of phenolic compounds in general and the expression of the genes involved in their synthesis during drought stress in Achillea pachycephala Rech.f. However, when analysing the individual identified phenolic compounds, the authors sometimes observed an initial reduction in their content and then an increase as the duration of the drought was extended. The patterns of gene expression were also slightly different. This indicates that drought affects the expression of key genes involved in the phenylpropanoid and flavonoid pathways as well as the accumulation of the compounds. Similar observations have been reported in the case of Amaranthus tricolor L. (Sarker and Oba, 2018). The polyphenol and flavonoid contents were elevated with an increase of the drought level.

3.4.4. Wounding

Wounding can induce the accumulation of phenolic compounds in plant tissue, connected with the activity of PAL genes. Increased PAL activity and the corresponding phenolic compound accumulation (mostly chlorogenic acid) have been observed in carrot (D. carota L.) after wounding (Surjadinata and Cisneros-Zevallos, 2012).

3.4.5. Temperature

In the experiment of Løvdal et al. (2010), tomato plants (Solanum lycopersicum L.) were treated with four temperatures: 12, 18, 24, and 30 °C. Next, the flavonoids and caffeoyl derivative content, as well as PAL activity and the expression of genes involved in the phenylpropanoid and flavonoid synthesis pathways were evaluated in leaves. Generally, a temperature of 12 °C stimulated the accumulation of anthocyanins and caffeoyl derivatives as well as PAL activity and the expression of most structural genes. Conversely, 30 °C reduced the phenolic compound content. In another work (Rezaie et al., 2020), sweet basil plants were treated with cold stress (4 and 10 °C) for 12, 24 and 48 h. In comparison to plants kept at room temperature, the treated plants accumulated more phenolic compounds in their leaves after 12 and 24 h of treatment. Cold stress stimulated the accumulation of phenolics, but the effect depended on how long the temperature was maintained (Rezaie et al., 2020).

3.4.6. Minerals

Løvdal et al. (2010) observed that nitrogen deficiency stimulated the accumulation of flavonoids and caffeoyl derivatives in tomato (S. lycopersicum L.) leaves. Also, the PAL activity and expression of the genes involved in flavonoid synthesis were higher in comparison to plants provided with a full nutrient solution (Løvdal et al., 2010). Nitrogen depletion usually increases polyphenol accumulation in leaves, and full nitrogen fertilization results in a reduction of phenolic compounds. In fruits, the reaction is not so obvious. Often, nitrogen fertilization does not affect phenolic accumulation in fruits. Sometimes, high nitrogen fertilization combined with a low dose of potassium or phosphorus causes the highest phenolic synthesis. In general, fertilization with nitrogen, phosphorus, and potassium affects the accumulation of phenolic compounds, and the reaction of leaves and fruits may be different (Heimler et al., 2017). Plants also have access to the ions of potentially toxic elements, heavy metals. An excess of heavy metal ions stimulates the accumulation of phenolic compounds by stimulating the expression of the genes involved in their synthesis (phenylalanine ammonia-lyase, chalcone synthase, shikimate dehydrogenase, cinnamyl alcohol dehydrogenase) and increasing the activity of enzymes (PAL, SKDH, G6PDH, and CADH). Increased phenolic biosynthesis helps plants to mitigate the stress effects of excess heavy metals (Sharma et al., 2019).

3.4.7. Salinity

In an experiment made by Ma et al. (2019), during the germination of hullless barley (Hordeum vulgare L.), salinity stress (60 mM NaCl) induced the accumulation of free phenolic compounds after four and six days of the stress. However, the activity of the enzymes involved in the phenolic biosynthetic pathway (PAL, C4H, 4CL, C3H, COMT, and F5H) and the expression of their genes did not correlate with each other. The increase in activity was observed in the absence of changes in expression or even decreased expression of a given gene (Ma et al., 2019). An increase in the phenolic compound content under salinity stress has also been observed in Amaranthus tricolor L. leaves (Sarker and Oba, 2018).

3.4.8. UV radiation

UV radiation affects plant growth, development, and metabolism, including the production of phenolic compounds. The studies of Carbonell-Bejerano et al. (2014) of grapevine (V. vinifera L.) indicated that UV radiation affects the composition of fruits. The total soluble phenolic acid content was higher in absence of UV radiation, but the accumulation of flavonols was reduced without exposure to these wavelengths. Interestingly, the anthocyanin content was similar in the fruits that were treated and not treated with UV radiation (Carbonell-Bejerano et al., 2014). In 2017, Moreira-Rodríguez et al. showed that a low dose of UVB radiation stimulated the accumulation of phenolic compounds (expressed as total) in broccoli (B. oleracea var. italica L.) sprouts after short-term treatment (2h exposure) compared to plants that were not treated (Moreira-Rodríguez et al., 2017). However, the influence of the UVB treatment differed among specific phenolic compounds, since both an increase and a decrease in the compounds were observed. Additionally, a broad spectrum of light, including UVA radiation (3% in the spectrum), stimulates the concentration of phenolic compounds in the leaves of aubergine (Solanum melongena L.) and tomato (S. lycopersicum L.) transplants compared to red and blue light in different compositions (Wojciechowska et al., 2020). In the experiment of Bantis et al. (2016), two cultivars of sweet basil (O. basilicum L.) were treated with four different light spectra emitted from LED lamps and with a fluorescent lamp (as control). Both cultivars accumulated significantly more phenolic compounds in shoots treated with LED lamps than under the fluorescent tube. The highest phenolic content was found in the plants grown under the LED lamp with a spectrum containing 1% of UV radiation. Light intensity was the same in all treatments (Bantis et al., 2016).

3.4.9. Visible light

In the work of Løvdal et al. (2010), the flavonol content in tomato leaves was higher in plants treated with high light levels than those treated with low light intensity (200 and 100 µmol m \(^{-2}\) s \(^{-1}\) PAR, respectively). PAL activity was also induced by high light levels, although the expression of PAL5 and PAL6 was unchanged. Interestingly, the expression of CHS2 was increased in high light levels (Løvdal et al., 2010).

Light can also modulate the expression of 4-coumarate-CoA ligase (4CL); upregulation of its expression has been observed (Lavhaie et al., 2018). Craver et al. (2017) found that higher light intensity (105 vs. 315 µmol m \(^{-2}\) s \(^{-1}\) ) positively affected the accumulation of anthocyanins in kohlrabi (B. oleracea var. gongylodes L.) microgreens. However, the phenolic compound content remained at a similar level in kohlrabi microgreens regardless of light intensity (Craver et al., 2017). Pérez-López et al. (2018) cultivated lettuce (L. sativa L.) with green and red leaves under two light intensities (400 and 700 µmol m \(^{-2}\) s \(^{-1}\) PAR). In ambient CO\(_2\) (400 ppm) the increased light intensity resulted in higher content of total phenols, total flavonoids, and total phenolic acids in both salad leaves, and higher cyanidin derivatives in the red cultivar. However, in elevated CO\(_2\) (700 ppm) conditions, the total phenol content decreased with the increase in light intensity (Pérez-López et al., 2018).

Not only light intensity, but also the quality of radiation regulates the amount of phenolic compounds in plants. Kim et al. (2014) report that...
blue light emitted from LED lamps increased the total phenolic and total flavonoid concentration in cherry tomato leaves in comparison to plants treated with fluorescent lamps (Kim et al., 2014). In the experiment of Zoratti et al. (2014), bilberry (Vaccinium myrtillus L.) plants were treated for a short period (48 h) with red, blue, far-red, and white light, as well as with dark conditions, during fruit developmental stage 2 (green fruit). The ripe fruits had similar amounts of most phenolic groups, regardless of treatment. What is interesting, the amount of anthocyanins in ripe fruits after the blue, red, and far-red light treatments was higher than after the white light treatment or dark conditions (Zoratti et al., 2014).

The authors observed increased expression of the genes connected with the flavonoid pathway after 12 h of monochromatic light treatment compared to the white light treatment or dark conditions. They conclude that even a short monochromatic light treatment during fruit ripening can induce the accumulation of anthocyanins in ripe fruits. Many other studies have found that blue light stimulates the accumulation of phenolic compounds, such as in sprouts of canola (Brassica napus L.) (Park et al., 2019), callus cultures of basil (O. basilicum L.) (Nadeem et al., 2019), pak choi (B. campestris L. var. chinensis var. communis) (Zheng et al., 2018), and Chinese kale sprouts (B. oleracea var. alboglabra Bailey) (Qian et al., 2016). Nadalini et al. (2017) observed that blue light from a LED lamp decreased the pelargonidin-3-glucoside content in strawberry (F. × ananassa Duchesne ‘Elisanta’) fruits. According to Amoozgar et al. (2017), blue LED, in comparison to white LED, decreased the total phenolic content in lettuce (L. sativa L.). Red light can also stimulate some phenolic compound accumulation. Nadeem et al. (2019) found the highest flavonoid content in callus cultures of basil grown under red LEDs. In callus cultures of Camellia japonica L. plants Jang et al. (2020) observed the highest accumulation of phenolics and flavonoids in mixed light: red and blue or red, blue, and green. An addition of far-red light to red and blue light (at an appropriate ratio) can also increase the phenolic compound content in lettuce (Lee et al., 2016). In the case of rice plant (O. sativa L.) leaves, it has been proposed that both red and blue light stimulate the synthesis of phenolic compounds (MohanTy et al., 2016). In the phytochrome signalling pathway, the participation of bHLH, ZnF and MYB TF has been suggested. What is more, in the cryptochrome pathway, WRKY, MYB, bHLH and ZnF are involved.

The question that often arises is what is the best red to a blue ratio (R:B) is. In the greenhouse cultivation of lamb’s lettuce (V. locusta L.) in winter, the best R:B ratio for supplementary radiation was 90:10B (Wojciechowska et al., 2015). However, for cultivation in autumn the best ratio was 70R:30B (Dutka and Liu, 2015). In this case, the efficiency of the reaction is dependent on the rate of their proteolysis, or even their intracellular distribution. Moreover, a reaction may be inhibited by its product (metabolite feedback regulation), as it is in PAL, for example, where the activity is downregulated by trans-cinnamate (Zhang and Liu, 2015). In both the studies mentioned above, LED lamps were only used as a supplement to solar radiation. However, LED lamps can also be used as the only light source for plants. In Chinese kale (B. oleracea var. alboglabra Bailey) cultivation, mixed red and blue radiation at different ratios was used and compared with white LEDs by Zhang et al. (2020). The mixed R and B light increased the total phenol and anthocyanins content in the Chinese kale leaves. The red to blue ratio of 6:3 was better than 8:1 when taking into account the accumulation of phenolic compounds in leaves and flower stalks (Zhang et al., 2020).

A lot of interesting research exists, but the answer is still not complete. Plant reactions are species- or even variety-specific, and further study is required to fully understand the topic.

4. Conclusions

Plants produce metabolites as a reaction to internal and external signals. Many factors contribute to the actual content of folates in the plant, from genetic to environmental ones. Folates concentration in plants differ within certain organs and tissues and change during the plant’s lifespan. Furthermore, it has been observed that folates production in plants depends on soil parameters, nutrient availability, temperature, and more. In addition, plants produce many phenolic compounds in response to stress factors. Increased accumulation of phenolic compounds has been observed as a result of stress caused by injury, cold, heat, drought, salinity, UV radiation, excessive visible radiation, hypoxia, mineral deficiency, excess heavy metals, and other phenomena (Agati et al., 2012; Caretto et al., 2015). On the one hand, treating plants with stress factors to obtain products with higher polyphenol concentrations may be a tempting idea. On the other hand, stress conditions may affect yield, as well as the accumulation of other phytochemicals, resulting in overall changes to biological and consumer value. It should be remembered that the synthesis and accumulation of such a large group of compounds as folates or polyphenols depend on many factors, which suggests a need to view these processes as very complex. In this mass of factors, however, it is worth paying attention to light, its quantity and quality. Manipulating light parameters while cultivating plants undercover is becoming easier and easier. The chain of reactions triggered by a given spectrum ends with concrete changes in plant morphology, physiology and/or metabolism. Therefore, according to some studies, light can be used as a growth regulator and exploited for practical application (Folta and Carvalho, 2015). It must be acknowledged that the development of light-emitting diode (LED) technology has contributed to the innovative use of specific light spectra to control the growth, development, and biochemical composition of plants (Dutta Gupta, 2017; Sipos et al., 2020). Bearing in mind the need to keep all growth factors at optimum levels, manipulation of light seems to be an easy and promising way to improve the content of the desired compounds in plants.

5. Future perspectives

Concentrations of folates and phenolic compounds in plants depend on both the efficiency of their biosynthesis and the rate of their degradation. The biosynthesis of phytochemicals is strongly affected by the activity of the enzymes involved in these processes, but also by the availability of substrates. Thus, undisturbed primary metabolism, including effective photosynthesis, is crucial to the optimal production of secondary metabolites since it is the source of these substrates. On the other hand, the activity of particular biosynthetic enzymes is modulated by their gene expression, post-transcriptional and post-translational processing, the rate of their proteolysis, or even their intracellular distribution. Moreover, a reaction may be inhibited by its product (metabolite feedback regulation), as it is in PAL, for example, where the activity is downregulated by trans-cinnamate (Zhang and Liu, 2015). In this case, the efficiency of the reaction is dependent on the rate of product depletion. Taking into account all these considerations, a question arises: up to what level can the accumulation of these compounds be stimulated by appropriate growing conditions? The results obtained so far and presented in this work are quite promising and indicate the possibility to increase the biological and health-beneficial value of plant-based foods sustainably by modulating growing conditions with particular involvement of light. Plant production all year round needs artificial light. It can be used to complement solar radiation or to replace it (growth chambers, vertical farms etc.). The production of healthy plant foods rich in folates and polyphenols requires the appropriate plant lighting. As shown in this review, it is difficult to define a universal light spectrum for enhancing folates or polyphenols synthesis across the entire range of plants. However, the results of using UV, blue or green light are very promising, and we emphasize the necessity for further research in this field.

Funding

This study was supported by The Ministry of Education and Science of the Republic of Poland, Subsidy SUB/2020–050012-D011 and Subsidy SUB2020-050014-D011. Institutional support was provided by Małopolska Centre of Biotechnology, Jagiellonian University.
CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Ahou-Sahle, M.T., Coper, A., 2006. Folic acid and the treatment of depression. J. Psychosom. Res. 61, 285–287. https://doi.org/10.1016/j.jpsychores.2006.07.007.

Agati, G., Azzarello, E., Pollastri, S., Tattini, M., 2012. Flavonoids as antioxidants in plant: location and functional significance. Plant Sci 196, 67–76. https://doi.org/10.1016/j.plants.2012.07.014.

Albani, D., Giorgetti, L., Pitto, L., Cantoni, R.M., Tattini, M., 2012. Flavonoids as antioxidants in plant: location and functional significance. Plant Sci 196, 67–76. https://doi.org/10.1016/j.plants.2012.07.014.

Delchier, N., Herbig, A.L., Rychlik, M., Renard, C.M.G.C., 2016. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Dlugosz-Grochowska, O., Kolton, A., Wojciechowska, R., 2016. Modifying folate and polyphenol concentrations in Lamb’s lettuce by the use of LED supplemental lighting during cultivation in greenhouses. J. Funct. Foods. 26, 228–237. https://doi.org/10.1016/j.jff.2016.07.020.

Fathi, E., Majidi, M., Dastan, D., Maroufi, A., 2019. The spatio-temporal expression of some genes involved in the biosynthetic pathways of terpenes/phenylpropanoids in yarrow (Achillea millefolium). Plant Physiol. and Biochem. 142, 43–52. https://doi.org/10.1016/j.plaphy.2019.06.036.

Galván, G.C., Fiehn, O., 2012. Sensing the light environment in plants: plant photoreceptors and early signalling steps. Curr. Opin. Neurobiol. 34, 46–53. https://doi.org/10.1016/j.conb.2015.01.013.

Gambonnet, B., Jabrin, S., Ravanell, S., Karam, M., Douce, R., Rebeille, F., 2001. Folate distribution during higher plant development. J. Sci. Food Agric. 81, 835–841. https://doi.org/10.1002/073526809.735.

Gambonnet, B., Jabrin, S., Ravanell, S., Karam, M., Douce, R., Rebeille, F., 2001. Folate distribution during higher plant development. J. Sci. Food Agric. 81, 835–841. https://doi.org/10.1002/073526809.735.

Galván, G.C., Fiehn, O., 2012. Sensing the light environment in plants: plant photoreceptors and early signalling steps. Curr. Opin. Neurobiol. 34, 46–53. https://doi.org/10.1016/j.conb.2015.01.013.

Genovesio-Grozowska, O., Kołton, A., Wojciechowska, R., 2016. Modifying folate and polyphenol concentrations in Lamb’s lettuce by the use of LED supplemental lighting during cultivation in greenhouses. J. Funct. Foods. 26, 228–237. https://doi.org/10.1016/j.jff.2016.07.020.

Hanson, A.D., Gregory, J.F., 2011. Folate biosynthesis, turnover, and transport in plants. Annu. Rev. Nutr. 31, 319–338. https://doi.org/10.1146/annurev.nutr.31.012810.135116.

Hilmy, M., Iqbal, M.S., Hashem, A., Abd_Allah, E.F., Ansari, M.I., 2021. Plant defense compounds. Eur. J. Biochem. 253, 251–262. https://doi.org/10.1111/1751-1092.13361.

Jare, M., Pihl, K., Põldma, J., Katus, T., 2015. Sensing the light environment in plants: plant photoreceptors and early signalling steps. Curr. Opin. Neurobiol. 34, 46–53. https://doi.org/10.1016/j.conb.2015.01.013.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.

Kołton, A., Renard, C.M.G.C., 2015. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.

Kołton, A., Renard, C.M.G.C., 2015. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.

Kołton, A., Renard, C.M.G.C., 2015. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.

Kołton, A., Renard, C.M.G.C., 2015. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.

Kołton, A., Renard, C.M.G.C., 2015. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.

Kołton, A., Renard, C.M.G.C., 2015. Folate in fruits and vegetables: contents, processing, and stability. Comp. Rev. Food Sci. Food Saf. 15, 506–528. https://doi.org/10.1111/1541-4379.12193.

Kołton, A., Ryczlik, M., Renard, C.M.G.C., 2013. Effects of industrial processing on folate content in green vegetables. Food Chem 139, 815–824. https://doi.org/10.1016/j.foodchem.2013.01.067.
Mandoulakani, B.A., Evyapour, E., Ghadimazadeh, M., 2017. The effect of drought stress on the expression of key genes involved in the biosynthesis of phenylpropanoids and essential oils in Thymus serpyllum. Int. J. Phytoremediation 19, 1–12. https://doi.org/10.1080/15592440.2016.1184455.

Mcdonald, K., 1999. Health-promoting components of organically versus inorganically grown fruits and vegetables. Subtropical Plant Sci 54, 23–28. https://doi.org/10.1016/S1371-9350(98)80062-0.

Ma, Y., Wang, P., Wang, M., Sun, M., Gu, Z., Yang, R., 2019. GABA mediates phenolic accumulation profile and gene expression pattern in tea plant (Camellia sinensis). PLoS ONE 4 (9), e00835. https://doi.org/10.1371/journal.pone.0083515.

Joshi, R., Adhikari, S., Parajuli, B.S., Chattopadhyay, S., Mukherjee, T., 2001. Free radical scavenging behavior of folate: evidence for possible antioxidant activity. Free Radic. Biol. Med. 30 (12), 1390–1399. https://doi.org/10.1016/S0891-5849(01)00245-7.

Jurenicka, A., Tam, T.T.T., Iani, V., Moan, J., 2013. The action spectrum for folic acid biosynthesis, classification, function and pharmacological properties. J. Pharm. Pharmacol. 2, 377–392.

Kawabata, K., Yoshioka, Y., Terao, J., 2019. Role of intestinal microbiota in the bioavailability and physiological functions of dietary polyphenols. Molecules 24 (2), 353. https://doi.org/10.3390/molecules24020353.

Kim, E.Y., Park, S.A., Park, B.J., Lee, Y., Oh, M.M., 2014. Growth and antioxidant phenolic compounds in cherry tomato seedlings grown under monochromatic light-emitting diodes. Int. J. Mol. Sci. 55 (6), 506–513. https://doi.org/10.1007/s13580-014-0121-7.

Kolton, A., Wojciechowska, R., Leja, M., 2011. Effect of maturity stage and year. J. Am. Soc. Hortic. Sci. 127, 843–847. https://doi.org/10.21273/hortsci.41.1.59.

Ko, S., Souli, S., Bolukbi, H., Ünsal, N., Gzenmen-Karadag, M., 2020. Obesity is associated with folate metabolism: a systematic review. Int. J. Nutr. Metab. Res. 90, 353–364. https://doi.org/10.1007/9810-000004.

Koyama, K., Roberto, S.R., de Souza, R.T., Borges, W.F.S., Anderson, M., Waterhouse, A., K, Kim, E.Y., Park, S.A., Park, B.J., Lee, Y., Oh, M.M., 2014. Growth and antioxidant phenolic compounds in cherry tomato seedlings grown under monochromatic light-emitting diodes. Int. J. Mol. Sci. 55 (6), 506–513. https://doi.org/10.1007/s13580-014-0121-7.

Kolton et al. Scientia Horticulturae 291 (2022) 110561

Kumar, N., Goel, N., 2019. Phenolic acids: Natural versatile molecules with promising therapeutic applications. Biotechnol. Rep 24, e00370. https://doi.org/10.1016/j.btre.2019.e00370.

Lavhale, S.G., Kalunka, R.M., Giri, A.P., 2018. Structural, functional and evolutionary diversity of 4-coumarate-CoA ligase in plants. Planta 248 (5), 1043–1057. https://doi.org/10.1007/s00425-018-3393-2.

Lazzarin, M., Meisburgen, M., Meijer, D., van Leuven, W., Marcelis, I.F.M., Kappers, I.F., van der Koot, A., van Loon, J.J.A., Dicke, M., 2021. LEDs make it resilient: effects on plant growth and defense. Trends Plant Sci. 26 (5), 496–508.

Lee, M.J., Son, K.H., Oh, M.M., 2016. Increase in biomass and bioactive compounds in lettuce under various ratios of red to far-red LED light supplemented with blue LED light. Hortic. Environ. Biotechnol. 57 (2), 139–147. https://doi.org/10.1007/s13193-015-0133-6.

Lester, G.E., 2006. Environmental regulation of human health nutrients (ascorbic acid, β-carotene, vitamins C, and folic acid) and vegetables. Horticult. Rev. 34, 59–64. https://doi.org/10.1207/s1533865xhr3401_5.

Lester, G.E., Crosby, K.M., 2002. Ascorbic acid, folic acid, and potassium content in lettuce. J. Food Com. 173, 143–152. https://doi.org/10.1021/c700111-0112-8.

Lougkachiai, R., Chaoaneshi, R., Kettawan, A., 2019. Vitamin C, folate, and phytochemical compounds of organically versus inorganically grown fruits and vegetables commonly consumed in Thailand. Pharm. Sci. Asia. 46, 218–230. https://doi.org/10.1016/j.psphar.2018.07.004.

Kore, S., Souli, S., Bolukbi, H., Unsali, N., Gzenmen-Karadag, M., 2020. Obesity is associated with folate metabolism: a systematic review. Int. J. Nutr. Metab. Res. 90, 353–364. https://doi.org/10.1007/9810-000004.

Koyama, K., Roberto, S.R., de Souza, R.T., Borges, W.F.S., Anderson, M., Waterhouse, A., L, Cantu, D., Fidelibus, M.W., Blanco-Ulate, B., 2018. Exogenous ascorbic acid promotes anthocyanin biosynthesis and increased expression of flavonoid synthesis genes in Viitis vinifera x Viitis labrusca table grapes in a subtropical region. Front. Plant Sci. 9, 322. https://doi.org/10.3389/fpls.2018.00521.

Liu, R.H., 2013. Health-promoting components of fruits and vegetables in the diet. Adv. Nutr. (3), 386S–392S.

Lavdal, T., Olsen, K.M., Slimestad, R., Verheul, M., 2014. Growth and antioxidant phenolic compounds in cherry tomato seedlings grown under monochromatic light-emitting diodes. Int. J. Mol. Sci. 55 (6), 506–513. https://doi.org/10.1007/s13580-014-0121-7.

Ma, Y., Wang, P., Wang, M., Sun, M., Gu, Z., Yang, R., 2019. GABA mediates phenolic accumulation profile and gene expression pattern in tea plant (Camellia sinensis). PLoS ONE 4 (9), e00835. https://doi.org/10.1371/journal.pone.0083515.

Mak, D.J., Lester, G., 2002. Effect of soil type, light intensity, and cultivar on leaf nutrients in mustard greens. Subtropical Plant Sci 54, 23–28.
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Scientia Horticulturae 291 (2022) 110561

Watanabe, S., Obtani, Y., Tatsukami, Y., Aeki, W., Ameniya, T., Sukekiyo, Y., Kubokawa, S., Ueda, M., 2017. Folate biofortification in hydroponically cultivated spinach by the addition of phenylalanine. J. Agric. Food Chem. 65, 4605–4610. https://doi.org/10.1021/acs.jafc.7b01375.

Weaver, L.W., Herrmann, K.M., 1997. Dynamics of the shikimate pathway in plants. Trends Plant Sci 2, 246–351.

Williamson, G., 2017. The role of polyphenols in modern nutrition. Nutr. Bull. 42 (3), 226–235. https://doi.org/10.1111/nbu.12278.

Winkel-Shirley, B., 2001. Flavonoid biosynthesis. A colorful model for genetics, biochemistry, cell biology, and biotechnology. Plant Physiol 126 (2), 485–493.

Wojcieszewska, R., Pizguez-Chowchowski, O., Kolton, A., Zupnik, M., 2015. Effects of LED supplemental lighting on yield and some quality parameters of lamb’s lettuce grown in two winter cycles. Sci Hortic 187, 80–86. https://doi.org/10.1016/j.scienta.2015.03.006.

Wojcieszewska, R., Kolton, A., Kunicki, E., Mrowiec, K., Barthel, P., 2020. LED lighting affected the growth and metabolism of eggplant and tomato transplants in a greenhouse. Hortic. Sci. (Prague) 47, 150–157. https://doi.org/10.17221/78/2019-HORTSCI.

Wusigale, Liang, L., 2020. Folates : Stability and interaction with biological molecules. J. Agric. Food Res. 2, 100039 https://doi.org/10.1016/j.jafres.2020.100039.

Xiong, E., Dong, G., Chen, F., Zhang, C., Li, S., Zhang, Y., Shihang, J.J., Yang, X., Zhou, Y., Qian, Q., Wu, L., Yu, Y., 2020. Formyl tetradehydrofolate deformylase affects hydrogen peroxide accumulation and leaf senescence by regulating the folate status and redox homeostasis in rice. Sci. China Life Sci. 63, 1–19. https://doi.org/10.1007/s11427-020-1677-3.

Xu, D., Zou, J., Fang, Y., Yan, Z., Shi, J., Gao, L., Wang, Q., Jiang, A., 2020. Effect of folic acid on the postharvest physiology of broccoli during storage. Food Chem 339, 127981. https://doi.org/10.1016/j.foodchem.2020.127981.

Yang, F., Li, W., Jiang, N., Yu, H., Morohashi, K., Ouma, W.Z., Morales-Mantilla, D.E., Gomez-Cano, F.A., Mukundi, E., Prada-Salcedo, L.D., Velazquez, R.A., Valentín, J., Mejía-Guerra, M.K., Gray, J., Doseff, A.L., Grotewold, E., 2017. A maize gene regulatory network for phenolic metabolism. Mol. Plant. 10, 498–515. https://doi.org/10.1016/j.molplant.2016.10.020.

Zhang, X., Liu, C.J., 2015. Multifaceted regulations of gateway enzyme phenylalanine ammonia-lyase in the biosynthesis of phenylpropanoids. Mol. Plant. 8, 17–27.

Zhang, Y., Ji, J., Song, S., Su, W., Liu, H., 2020. Growth, nutritional quality and health-promoting compounds in Chinese kale grown under different ratios of red: blue LED lights. Agronomy 10 (9), 1248. https://doi.org/10.3390/ajms091248.

Zhao, L., Gao, L., Wang, H., Chen, X., Wang, Y., Yang, H., Wei, C., Wan, X., Xia, T., 2013. The R2R3-MYB, bHLH, WD40, and related transcription factors in flavonoid regulatory network for phenolic metabolism. Mol. Plant. 10, 2245–2256. https://doi.org/10.1093/mp/sst100.

Zheng, Y., Cantley, L.C., 2019. Toward a better understanding of folate metabolism in health and disease. J. Exp. Med. 216, 253–266. https://doi.org/10.1084/jem.20181965.

Zheng, Y.J., Zhang, Y.T., Liu, H.C., Li, Y.M., Liu, Y.L., Hao, Y.W., Lei, B.F., 2018. Formyl tetrahydrofolate deformylase affects hydrogen peroxide accumulation and leaf senescence by regulating the folate status and redox homeostasis in rice. Sci. China Life Sci. 63, 1–19. https://doi.org/10.1007/s11427-020-1677-3.

Zhou, Y., Qian, Q., Wu, L., Yu, Y., 2020. Formyl tetradehydrofolate deformylase affects hydrogen peroxide accumulation and leaf senescence by regulating the folate status and redox homeostasis in rice. Sci. China Life Sci. 63, 1–19. https://doi.org/10.1007/s11427-020-1677-3.