REVIEW ARTICLE



Phenylpropanoid Derivatives and Their Role in Plants' Health and as antimicrobials

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Abstract

Phenylpropanoids belong to a wide group of compounds commonly secreted by plants and involved in different roles related with plant growth and development and the defense against plant pathogens. Some key intermediates from shikimate pathway are used to synthesize these compounds. In this way, by the phenylpropanoid pathway several building blocks are achieved to obtain flavonoids, isoflavonoids, coumarins, monolignols, phenylpropenes, phenolic acids, stilbenes and stilbenoids, and lignin, suberin and sporopollenin for plant–microbe interactions, structural support and mechanical strength, organ pigmentation, UV protection and acting against pathogens. Some reviews have revised phenylpropanoid biosynthesis and regulation of the biosynthetic pathways. In this review, the most important chemical structures about phenylpropanoid derivatives are summarized grouping them in different sections according to their structure. We have put special attention on their different roles in plants especially in plant health, growth and development and plant-environment interactions. Their interaction with microorganisms is discussed including their role as antimicrobials. We summarize all new findings about new developed structures and their involvement in plants health.

Introduction

Phenylpropanoids are a wide class of natural compounds, which are synthesized by plants from phenylalanine or tyrosine, through a series of enzymatic reactions. Their name is derived from the six-carbon, aromatic phenyl group and the three-carbon propene tail of coumaric acid. The biosynthesis begins with phenylalanine, which is first converted to cinnamic acid by the action of the enzyme phenylalanine ammonia-lyase (PAL). Hydroxylation of cinnamic acid in the 4-position, by trans-cinnamate 4-monooxygenase, leads to p-coumaric acid. *p*-Coumaric acid is transformed with coenzyme A to give 4-coumaroyl-CoA, which is the central intermediate in phenylpropanoid biosynthesis. From this 4-coumaroyl-CoA emanates the biosynthesis of myriad natural products, which can be divided into several groups including flavonoids and isoflavonoids, coumarins, monolignols, phenylpropenes, phenolic acids, stilbenes and stilbenoids, and sporopollenin as shown in Fig. 1 [1].

Estibaliz Sansinenea estisansi@yahoo.com.mx Phenylpropanoids contribute to all aspects of plant responses toward biotic and abiotic stimuli. They are not only indicators of plant stress responses upon variation of light or mineral treatment but are also key mediators of the plants' resistance toward pests. Some of them even contribute to the stability and strength of the plant against environmental damage [2]. The wide applications are due to the diversity of phenylpropanoids structures derived from shikimate pathway with the core structure of phenylalanine as central structure. This diversity in structures is achieved through a set of enzymes including lyases, transferases, ligases, oxygenases, and reductases, many of which are encoded by gene superfamilies [3].

Phenylpropanoids are involved in several plant functions, such as providing color to flowers, fruits, grains, and vegetables, protecting plants from UV radiation, protecting plants from environmental stresses and against pathogens and acting as signaling molecules to facilitate nitrogen fixation and seed dormancy [4, 5]. Besides, these compounds have attracted attention due to their benefits on human health [6].

There are some interesting reviews about these compounds [1, 3], but are mainly focused on the phenylpropanoid biosynthesis and regulation of the biosynthetic pathways putting special attention on their structures and enzymes that are crucial

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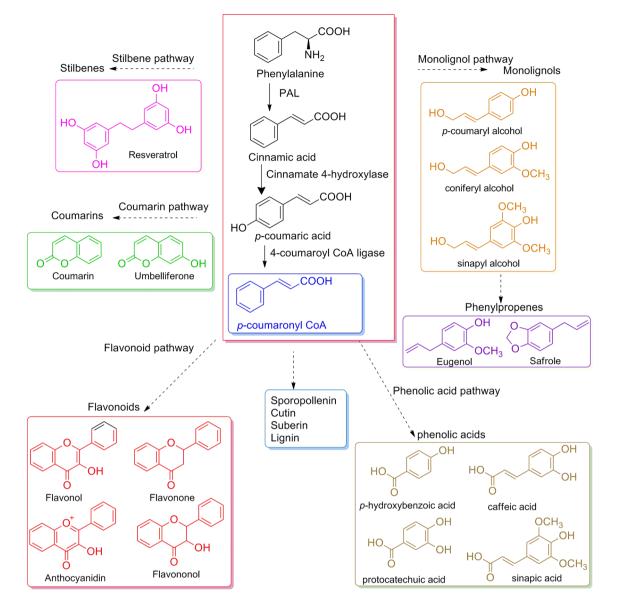


Fig. 1 Diversification of Phenylpropanoids and representative chemical structures based on the general Phenylpropanoid Pathway

in the biosynthesis of them, without emphasizing on the role they play in plant defense or growth. With this aim in mind in this review we describe the phenylpropanoid derivatives highlighting their structures but putting attention on their role in plants, especially in plant health, growth and development and plant-environment interactions. We summarize all new findings about new developed structures and their involvement in plants health. We have emphasized on the role of phenylpropanoids against microorganisms, phytopathogenic or human pathogens, acting as antimicrobials.

Flavonoids, Isoflavonoids Characteristics and Their Role in Plants

Flavonoids are the most abundant in plants. The chemical structure of flavonoids consists of a diphenylpropane, containing a fifteen-carbon skeleton, with two phenyl rings linked via a three-carbon chain abbreviated as C6–C3–C6 [7]. According to the variations in the heterocyclic ring flavonoids can be divided in several groups such as flavones,

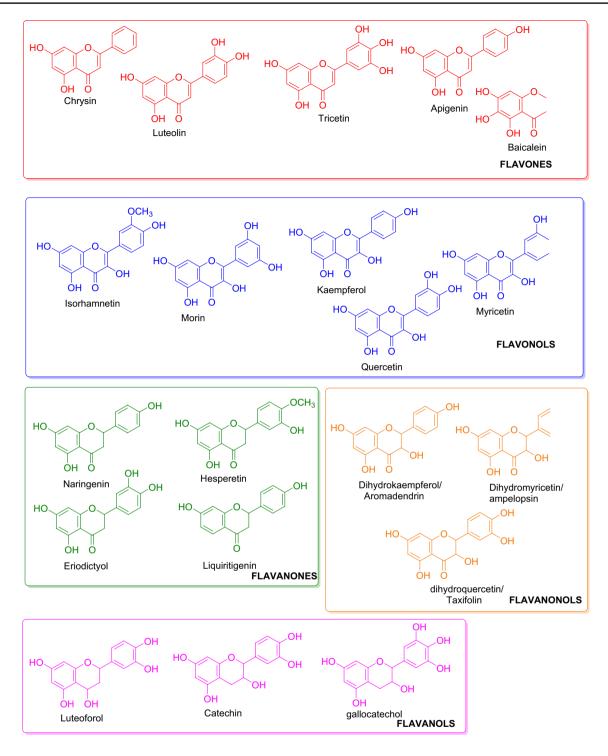


Fig. 2 The main flavonoids

flavonols, flavanones, flavanonols, and flavanols as main flavonoids, as shown in Fig. 2 [8].

In minor proportion, there are some other flavonoids such as aurones, auronols, and anthocyanidins [3, 9, 10]. Among the isoflavonoids we can found isoflavones, isoflavanones, and isoflavanols [11, 12]. The structures of flavonoids are usually glycosylated, since glycosides have greater solubility and mobility in plants. Besides, glycosylated forms do not interfere with vital cellular mechanisms [13, 14].

Flavonoids have important roles in plant growth, since they are produced as a response to developmental signals during seed development and to environmental signals, for crops' protection against biotic and abiotic stresses [3]. Flowers usually display bright and contrasting colors to attract pollinators and facilitate the reproductive success of the species. The presence and interaction of flavonoids in plants contribute to the color of them. Flavonoids often exhibit some colors to supply pigmentations to flowers, fruits, and seeds to attract pollinators and seed dispersers [15]. Anthocyanins can be found ranging from orange to pink, red, and purple while aurones are bright yellow [16]. Flavones and flavonols function as co-pigments of anthocyanins and increase the intensity, stability, and diversity of colors [17]. A high concentration of total flavonols and moderate amounts of anthocyanins contribute to the formation of pink petals, while orange petals exhibit a high content of total anthocyanins and a low content of total flavonols [18]. The function of pigments also involves the protection against UV radiation. Plants subjected to high UV-B irradiation, register high levels of flavone glucosides [19].

Flavonoids have a role in plants' fertility, since the pollen grains, which are crucial structures for plant reproduction, are covered by flavonoid glycosides [20]. In addition, flavones and isoflavones can act as chemo attractants and/or as inducers of nitrogen-fixing root nodule formation [21].

One of the most widely publicized properties of flavonoids is their capability to scavenge reactive oxygen species (ROS). Although this has been known for some time, flavonoids are gaining more and more notoriety due to the impact of ROS on plant metabolism and physiology [22]. Flavonoids reduce oxidative damage caused by reactive oxygen species (ROS) that is induced by abiotic stresses such as soil salinity, drought, and extreme temperatures [23, 24].

Stilbenes and Stilbenoids as Defense Mechanisms of Plants

Stilbenes are synthesized in plants as a defense mechanism, acting as phytoalexins, against external stresses such as pathogenic attack/infection and UV radiation [25]. The main stilbene structures are derived from resveratrol, which retards the aging process and increases the longevity in various organisms [26]. Besides, stilbenes have interesting healthpromoting properties that benefit to human health [27–29]. These compounds are isolated from several plants' families mainly peanuts, grapes, bilberries, blueberries, purple grapes, and cranberries, among others [30]. Stilbenes are a class of phenolic compounds containing 14 carbons, where a double-bonded ethylene bridge links the two phenyl rings. One phenyl ring carries two hydroxyl groups, while the other ring carries substituted hydroxyl or methoxy groups in different positions [31]. These compounds can occur in free form, prenylated, geranylated, or glycosylated form and in monomeric or polymeric (dimeric, trimeric, or others) forms. More than 300 resveratrol oligomers, usually containing two to eight resveratrol units, have been characterized, which are formed through oligomerization of the resveratrol monomers [32].

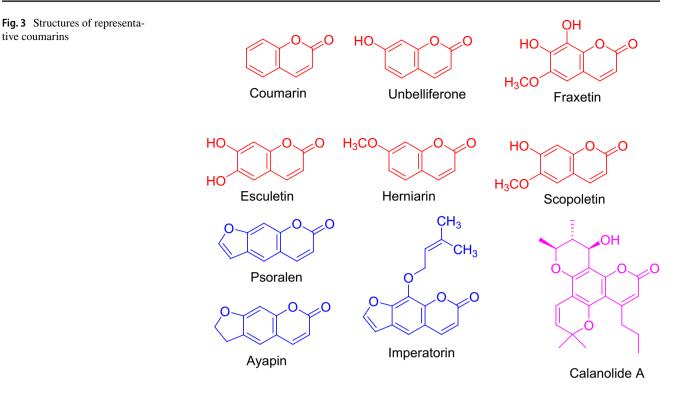
The isolation and extraction of these compounds are mainly carried out using methanol as a solvent and in the dark. *Trans*-isomer easily isomerizes to the *cis* form in solution as it is not stable when exposed to light, while the opposite path is induced by heat or light. Their identification can be done for the known stilbenes, comparing retention time and MS or MS/MS data with standards, and for the unknown ones, using NMR, IR, MS, and UV–Vis [33].

In addition to their essential roles in plants, stilbenes have shown broad pharmacological and biological activities. Resveratrol has been one of the most demanded that has been applied in pharmaceutical, food, and cosmetic industries [31].

Coumarins as Chemical Defense to Discourage Predation

Coumarins are a large class of naturally occurring phenylpropanoids and/or synthetic oxygen-containing heterocycles, bearing a typical benzopyrone framework with the fused backbone of benzene and α -pyrone ring (α -benzopyrones). Coumarin was first isolated from tonka beans (Dipteryx odorata) and has been described in natural products, organic chemistry, and medicinal chemistry. It has a sweet odor, easy to be recognized as the scent of new-mown hay; therefore, coumarin has been used in perfumes since 1882. It is produced by plants as chemical defense to discourage predation, since coumarin has appetite-suppressing properties, which may discourage animals from eating plants that contain it. Though the compound has a pleasant-sweet odor, it has a bitter taste, and animals tend to avoid it. Plant coumarins can be divided into four groups, including simple coumarins, furanocoumarins, pyranocoumarins, phenylcoumarins, dihydrofurocoumarins, and biscoumarins [3]. Simple coumarins include coumarin, umbelliferone (7-hydroxycoumarin), scopoletin (7-hydroxy-6-methoxycoumarin), and esculetin (6,7-dihydroxycoumarin), as shown in Fig. 3.

They might also be found in glycosides form, including psoralen core-related structures. They are characterized by UV light absorption, resulting in a very characteristic blue fluorescence; they are also very photosensitive as they can be altered by natural light [34]. Coumarins are either stored within the plant cells as glycosylated conjugates to avoid toxicity or secreted into the rhizosphere as aglycones such as scopoletin, fraxetin, or esculetin [35]. Within the plant cells, coumarins accumulated in the vacuole are present in different plant organs including leaves, fruits, flowers, and roots, but also in the exudates of plants roots [36].



Coumarins play a role in iron deficiency, since a phenolics' release occurs when plants are experiencing iron limitation, facilitating the mobilization of sparingly available iron from the rhizosphere soil and the uptake by plant roots [37, 38]. This capacity of coumarins depends on the presence of a catecholic moiety in their structure, which resembles the structure of microbial catechol-type siderophores that function in the chelation and uptake of iron [39].

Coumarins function as phytoalexins, which are antimicrobial compounds that contribute to plant disease resistance against microbial pathogens. Studies in many different plant species have shown that coumarins can accumulate in response to infection by a diversity of pathogens. The antimicrobial activity of coumarins was found to depend on the number and the polarity of the oxygen substituents in the benzene ring [36]. The action mechanism through these compounds act against pathogens is varied and can be through direct effects on microbial membrane integrity or scavenging of reactive oxygen species (ROS) that are produced in response to pathogen infection and help to prevent tissue damage [40].

In agriculture, several elicitors, such as bacterial flagellin and fungal chitin, can be applied to enhance the defense potential of plants against various pathogens [41]. Some hormones, such as salicylic acid and jasmonic acid, can be elicitors of coumarins [42]. By the other side coumarins have a role in microbiome-root-shoot communication stimulating plant immunity [38].

Monolignols and Lignin Giving Resistance to the Wood of Trees

Monolignols are called hydroxy cinnamyl alcohol monomers, such as p- coniferyl alcohol, sinapyl alcohol, and coumaryl alcohol, containing C6–C3 skeleton. They differ from each other in the degree of methoxylation at C3 and C5 positions of the aromatic ring. The biosynthesis of monolignols is initiated from the general phenylpropanoid pathway, as was shown in Fig. 1. These compounds are building blocks of lignin and lignan.

Lignin is primarily produced from dehydrogenative polymerization of three monolignols through ether and carbon–carbon linkage [43]. Under the catalysis of laccase or peroxidase, monolignols are polymerized to form the corresponding lignin polymers, termed guaiacyl (G), sinapyl (S), and hydroxyl–coumaroyl (H) units, respectively. Lignin is the main structural component of cell wall in vascular plants to provide structural support Besides it is a physical barrier for pathogens and helps in water transport and nutrition assimilation. Lignin composition varies between plant species and tissues being normally richer in G units in gymnosperms and related species, richer in G and S units in dicot species, whereas monocot species usually have higher H unit content [44].

Lignans are formed by coupling two units of monolignols, typically two coniferyl alcohol units. Lignans play a role in the durability, longevity, and resistance of the heart wood of many tree species against some pathogenic fungi [45]. Similarly, they have a role in plants defense; however, they have received considerable interest based on pharmacological properties, such as in the case of the cytostatic, anti-inflammatory, antioxidant, anti-microbial, anti-obesity, and anti-cancerous [3].

Phenolic Acids for the Development, and Defense of Plants

These compounds are a large group of aromatic acid compounds containing the benzene ring linked with one or more hydroxyl or methoxy groups, which can be divided into the hydroxycinnamic acid group and the hydroxybenzoic acid group [46, 47]. Some of these compounds can be found in Fig. 4.

Phenolic acids are present in many consuming foods such as potato, onion, mushroom, apple, peach, wheat, tea, and coffee which are well known for their nutritional phenolic acid ingredients [48]. These compounds offer antioxidant capacity, which helps to prevent diabetes, cardiovascular diseases, and cancers. Their benefits for human health are invaluable; however, they also exhibit diverse biological functions in plants, which are the main focus of this review. Phenolic acids help with the plant growth, development, and defense against pathogen attacks, and work as signaling molecules during the initiation of arbuscular mycorrhizal establishment and legume rhizobia symbioses [49]. Phenolics are often produced and accumulated in the subepidermal layers of plant tissues exposed to stress and pathogen attack. Some factors, including trauma, wounding, drought, and pathogen attack, affect the synthesis and accumulation of phenolics

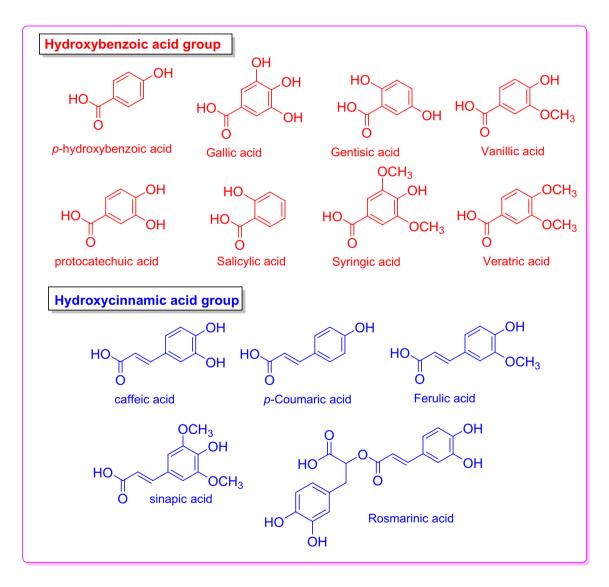


Fig. 4 Structures of phenolic acids

[50]. They act as protective agents, inhibitors, natural animal toxicants, and pesticides against invading organisms.

Phenylpropanoid Polymers: Suberin, Cutin, and Sporopollenin as Rigid Scaffolds

These polymers have different functions since they can serve as a water barrier for the sessile plant in case of suberin and cutin, or as a highly protective and rigid scaffold for the male gametophyte. These complex, variable, and highly rigid structures are based on only two building blocks, one aliphatic and another aromatic, and the second is lower than in the case of lignin. The production of suberin is limited to a few plant tissues, and its main components have been established as feruloyl esters. These esters are virtually absent in cutin [1].

The pollen cell wall is divided into exine and intine. The exine is highly resistant to chemical reagents and enzymes. The term sporopollenin describes the entire resistant material of exine. Apparently contains similar building blocks compared to cutin and suberin, namely phenylpropanoids including *p*-hydroxybenzoate, *p*-coumarate, ferulate, lignin guaiacyl, and hydroxylated fatty acids. In contrast to cutin and suberin, this polymer is even more resistant to chemical degradation, although advances in chemical analysis have enabled the complete identification and separation of its constituents [51].

New Phenylpropanoids Derivatives with Different Roles in Plants

The discovery of new natural compounds with biological activities has been a research topic during years and the isolation of new phenylpropanoids has not been the exception. Therefore, besides the typical compounds that have been described in preceding sections, there are new phenylpropanoid derivatives that have been described during the last years.

Cuendet and co-workers described in 2001 four phenylpropanoid derivatives called barbatosids A–D and a new catechin called barbatoflavan which were isolated from *Campanula barbata* [52]. Jiang and co-workers in 2017, described five phenylpropanoid derivatives, named as xanthiumnolics A–E, which were isolated from fruits of *Xanthium sibiricum* Patr [53]. Guo and co-workers in 2019 described six new phenylpropanoid derivatives called crataegusanoid A–F, which were isolated from the fruit of *Crataegus pinnatifida* Bunge [54]. In the same year Ma and co-workers described four new phenylpropanoid derivatives from *Murraya koenigii* [55]. Zhao and co-workers in 2021 described eight new phenylpropanoid derivatives called lyciruthephenylpropanoid A–G and 1-dehydroxy-1-carboxyl-breynioside A which were isolated from the fruits of *Lycium ruthenicum* Murr. (black wolfberry) [43]. Very recently, Xia and co-workers have isolated four new phenylpropanoid derivatives called xanthiifructins A–D from the fruits of *Xanthium sibiricum* [56].

Roles of Phenylpropanoids in Plants

As it has been mentioned before, phenylpropanoids are involved in several metabolic and physiological processes related to growth and development in plants, such as pollen tube germination and growth or seed maturation, dormancy and longevity and cell division. They are also involved in plant attractiveness to pollinators through the color or scent they confer to flowers synthesizing photosynthetic pigments. They also play a role in plant–microorganism communication for the establishment of symbiosis, such as in legume–rhizobium interactions during nodulation Phenylpropanoid derivatives have a role in root-shoot communication stimulating plant immunity [38].

However, they can also have defense responses in adverse abiotic or biotic conditions. When the pathogens act against plants, hitting the cell wall, phenylpropanoid pathway is triggered for plant defense. Several phenylpropanoid compounds are synthesized acting as antimicrobial compounds as well as signaling molecules. These compounds are regulated by hydroxycinnamic acids and monolignols through various complex mechanisms, which are still poorly described in plant science. Most of the articles establish the biosynthetic pathways of phenylpropanoids, highlighting the enzymes participating in these pathways [57].

The basal defense mechanism starts with the cell wall lignification, which increases the resistance capabilities of the cell wall by generating mechanical pressure during fungal attack and penetration. This process, establishes a mechanical barrier to pathogen attack, modifies the chemical composition of cell wall and produces toxic compounds, and free radicals against pathogens [58]. The role of phenylpropanoids as metabolites that may suppress the pathogenicity of pathogens has been studied as well as phenylpropanoids biosynthesis pathway and their regulation, but the mechanisms involved in the process have not been well established. However, there are recent reviews about phenylpropanoids response against some abiotic and biotic stresses [57–59]

These compounds can help to nutrient uptake through chelation of metallic ions, enhanced active absorption sites, and soil porosity with accelerated mobilization of elements like calcium (Ca), magnesium (Mg), potassium (K), zinc (Zn), iron (Fe), and manganese (Mn) [59].

Phenylpropanoids can fix nitrogen in legumes since they are involved in Nod factors synthesis. In general, they exert

positive effects in seed germination and intensify the photosynthetic activity; however, some phenylpropanoid compounds can be potentially phytotoxic if accumulated in high quantity and can inhibit germination and seedling growth [59].

In addition, phenylpropanoids have a role against some abiotic stress like heavy metals, drought, salinity, temperature, pesticides, and UV radiations. Heavy metals generate harmful ROSs causing oxidative stress, toxicity, and retarding growth of the plants. Flavonoids can enhance the metal chelation process reducing the levels of harmful hydroxyl radical in plant cells and can eliminate H_2O_2 enhancing a plant's resistance to heavy metals [60]. Some phenylpropanoids, such as flavonols, are stimulated under water deficit enhancing resistance against drought stress and modulating phenylpropanoid biosynthetic pathway [61]. Salinity generates ROS like substances, which cause oxidative stress to the plant. Phenolic compounds have powerful antioxidant properties and help in scavenging of harmful ROS in plants under salt stress [62]. It is known that UV-B radiations cause harmful mutations to DNA and generate ROS. Phenylpropanoid derivatives accumulated in plant can protect plants by making a shield under epidermal layer, absorbing UV radiations, and preventing dimerization of thymine along with reducing photodamage of important enzymes [63, 64]. Under temperature stress (both heat and chilling), plants phenylpropanoids, such as anthocyanins, flavonoids, flavonols, and phenolic acids, increase to protect plant cells [65]. In a similar way, phenylpropanoids accumulate in plants growing under pesticide stress conditions, which confer resistance to survive against pesticide toxicity [66]. In the Fig. 5 it has been shown the different phenylpropanoids, which are involved in plant growth and development and plant defense that are stimulated and produced by the plant against different abiotic and biotic stresses.

Biological Effects of Phenylpropanoids on Microorganisms

It has been mentioned the extensive roles that phenylpropanoids play in plants helping with the development and the growth of them, even having a role against some abiotic stresses. However, these amazing compounds have demonstrated that can act against a broad spectrum of microorganisms including phytopathogenic bacteria, fungi, and yeast [57]. Indeed, some of these compounds can be antimicrobials against human pathogens and food spoilage microorganisms [67].

Protection Against Phytopathogenic Microbes

According to several studies, phenylpropanoids and their derivatives can offer plant protection against some pathogens. This protection can be due to the defense elicitation of the host rather than having any significant toxicity against the microorganisms [68]. There are some examples where phenylpropanoid quantity increases in infected plants. In tobacco plants infected with Pseudomonas syringae flavonoids and other phenylpropanoid derivative content was increased [69]. Similarly, flavonoid glycosides and hydroxycinnamic acid production significantly increased in orange leaves infected by Candidatus *liberibacter asiaticus* [70]. Some studies have shown that carrot strains resistant to Alternaria dauci contained significantly higher levels of feruloylquinic acid, as well as 4-O- and 7-O-glycosides of apigenin, luteolin, and chrysoeriol, compared to susceptible genotypes [71]. In potato tubers enriched in rutin and nicotiflorin compounds, it has been seen resistance against Pectobacterium atrosepticum, and at the same time susceptible to Phytophthora infestans, a biotrophic fungal pathogen [72]. In maize plants an increase of ferulic acid compound was related with resistance against two phytopathogenic fungi such as Fusarium graminearum and Fusarium verticillioides. The accumulation of flavonoids in the context of disease resistance in various plants is described in many studies [59]. The antifungal activity, exerted by phenylpropanoids and flavonoids, has been investigated, corroborating their link to disease resistance. However, little is known about the mechanisms by which these compounds act against phytopathogens. Some studies have assessed the effect of phenylpropanoid derivatives on the integrity of plant fungal pathogens [59]. About viral pathogens, specific attention has been paid to the tobacco mosaic virus (TMV) in the exploration of the antiviral activity of candidate specialized metabolites, being quercetin and kaempferol the compounds that trigger the defense response of the host plant [73].

Protection Against Human Pathogens

Considering the importance of pathogens for human health it is not strange that there are many studies about the role of these compounds against human pathogens. For example, flavonoid glycosides were reported to cause cell lysis in *S. aureus* due to alteration of membrane permeability [74]. This can be explained through the physicochemical properties of phenylpropanoids, which are involved in their ability to cross the bacterial wall and lipidic membranes to reach their intracellular targets [75]. At this point it should be mentioned the main difference between gram-positive and gram-negative bacteria, since Gram-negative bacteria

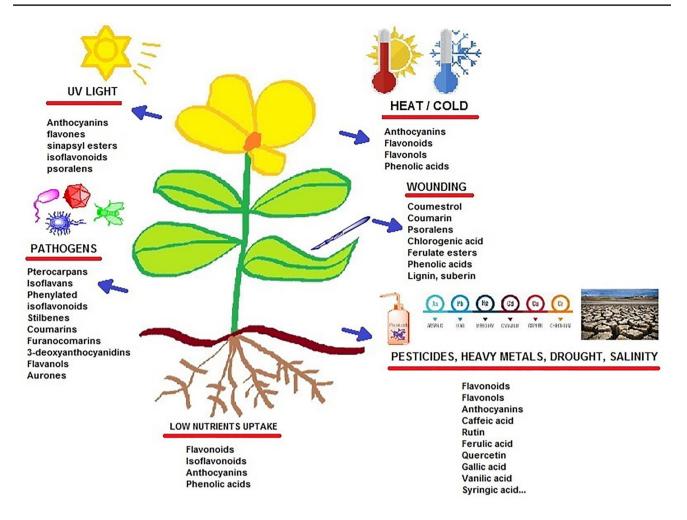


Fig. 5 Phenylpropanoids involved in plant growth and development and plant defense

have additional outer membrane with lipopolysaccharides anchored in it, making these bacteria less permeable to more compounds. This is the reason why these compounds have different antimicrobial activity against different bacteria [76]. Phenylpropanoid derivatives such as *p*-hydroxycinnamic acid methyl ester have been reported as a potent antibacterial compound against *Proteus vulgaris* and *Bacillus cereus*, comparable with a standard antibiotic, ampicillin [77]. About fungal pathogens it has been described that caffeic acid inhibits the growth of *C. albicans* [78]. Phenylpropanoids and their derivatives also possess antiviral activity against influenza virus [79], H1N1 virus [80], hepatitis C virus [81], and canine distemper virus [82].

Phenylpropanoids as Antimicrobials

It is remarkable that multi-drug resistant bacteria have been directly linked to thousands of deaths annually worldwide being a growing problem. To solve this problem natural products have received the attention due to their diverse structures and biological activities. In the previous section it has been mentioned that phenylpropanoids and their derivatives have antimicrobial activity against human pathogens, therefore they can be used to combat multi-drug resistant bacteria [83].

In contrast to the scarce information on the mechanisms involved in the action of phenylpropanoids against plant pathogens, there is more information on the mechanisms involved against human pathogens. One of the most common studied mechanisms of phenylpropanoids against both gram-positive and gram-negative bacteria is membrane disruption. However, currently one question is still open about whether the compound altered membrane stability by interfering with intracellular processes or by direct interaction with membrane components. The effect of gallic and ferulic acids was proved, observing that both acids increase surface hydrophilicity of Gram-negative bacteria and hydrophobicity of Gram-positive bacteria [84]. However, this surface hydrophilicity increase can be due to direct interaction with membrane or by interfering with intracellular components. Model membranes have already been used to test the direct interaction of epicatechin gallate and epigallocatechin gallate with membranes [85]. Nevertheless, the diversity of bacteria membrane composition is wide; therefore, specific studies are needed for each compound-pathogen interaction. The effects of eugenol, carvacrol, and thymol were observed to increase major fatty acids in Gram-negative bacteria, while Gram-positive *S. aureus* lipid profiles changed across several fatty acids. These results require interpretation but can give more information than membrane disruption assays.

There are also non-membrane action mechanisms, such as DNA intercalation, DNA gyrase inhibition, Type III secretion inactivation, dehydratase inhibition (HpFabZ), and protein kinase inhibition, among others [83]. It has been seen that multiple mechanisms can be simultaneously detected for one simple compound that is the case for quercetin compound. The most specific interaction details were found by the two studies that obtained crystal structures of quercetin or apigenin bound to the enzymes they inhibited [86, 87].

Synergistic effects have already been observed for many phenolic compounds when combined with antibiotics currently in use [88]. This synergism can be explained by the fact that phenylpropanoids and derivatives are membrane disrupting compounds that help antibiotics to access easier into the cell. Besides, some phenylpropanoids can block the efflux pumps, which are used to remove bacterial toxic compounds, to give access to the antibiotic compound for synergistic killing [89].

Conclusion

The chemical structural diversity of phenylpropanoids results from several core structures derived from shikimate pathway. As it has been seen along this review there are several classes of phenylpropanoid derivatives grouped by structure type. All of them are essential for plant growth, each of them providing different strategies to benefit the health and growth of the plant. Some of the benefits are known such as, antioxidant properties or synthesis of pigments, which can be chemo attractants or repellents for predators. However, it is interesting to know phenylpropanoids roles against abiotic stresses. It is important to highlight that phenylpropanoids and derivatives act against many microorganisms some of them are phytopathogens and others are human pathogens. The mechanisms of action of most naturally derived phenolic compounds are not well-characterized, although the main mechanism is membrane disruption. In this review, we can try to summarize the last advances in new derivatives and new functions of phenylpropanoids derivatives discovered in the last years.

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Author Contributions AO: Writing—review & editing. ES: Supervision, Writing—review & editing.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

References

- Vogt T (2010) Phenylpropanoid biosynthesis. Mol Plant 3:2–20. https://doi.org/10.1093/mp/ssp106
- Bais HP, Vepachedu R, Gilroy S, Callaway RM, Vivanco JM (2003) Allelopathy and exotic plant invasion: from molecules and genes in species interaction. Science 301:1377–1380. https://doi. org/10.1126/science.1083245
- Deng Y, Lu S (2017) Biosynthesis and regulation of phenylpropanoids in plants. Crit Rev Plant Sci 36:257–290. https://doi.org/ 10.1080/07352689.2017.1402852
- Subramanian S, Stacey G, Yu O (2007) Distinct, crucial roles of flavonoids during legume nodulation. Trends Plant Sci 12:82–85. https://doi.org/10.1016/j.tplants.2007.06.006
- Gu XY, Foley ME, Horvath DP, Anderson JV, Feng J, Zhang L, Mowry CR, Ye H, Suttle JC, Kadowaki K, Chen Z (2011) Association between seed dormancy and pericarp color is controlled by a pleiotropic gene that regulates abscisic acid and flavonoid synthesis in weedy red rice. Genetics 189:1515–1524. https://doi. org/10.1534/genetics.111.131169
- Dwivedi SL, Upadhyaya HD, Chung IM, DeVita P, García-Lara S, Guajardo-Flores D, Gutiérrez-Uribe JA, Serna-Saldívar SO, Rajakumar G, Sahrawat KL, Kumar J, Ortiz R (2016) Exploiting phenylpropanoid derivatives to enhance the nutraceutical values of cereals and legumes. Front Plant Sci 7:763. https://doi.org/10. 3389/fpls.2016.00763
- Tohge T, de Souza LP, Fernie AR (2017) Current understanding of the pathways of flavonoid biosynthesis in model and crop plants. J Exp Bot 68:4013–4028. https://doi.org/10.1093/jxb/erx177
- Kumar S, Pandey AK (2013) Chemistry and biological activities of flavonoids: an overview. Sci World J 2013:162750. https://doi. org/10.1155/2013/162750
- Ali HM, Almagribi W, Alrashidi MN (2016) Antiradical and reductant activities of anthocyanidins and anthocyanins, structureactivity relationship and synthesis. Food Chem 194:1275–1282. https://doi.org/10.1016/j.foodchem.2015.09.003
- Smeriglio A, Barreca D, Bellocco E, Trombetta D (2016) Chemistry, pharmacology and health benefits of anthocyanins. Phytother Res 30:1265–1286. https://doi.org/10.1002/ptr.5642
- Foudah AI, Abdel-Kader MS (2017) 'Isoflavonoids'. In: Justino GC (ed) Flavonoids-from biosynthesis to human health. IntechOpen, London. https://doi.org/10.5772/intechopen.68701
- Nakayama T, Takahashi S, Waki T (2019) Formation of flavonoid metabolons: functional significance of protein-protein interactions and impact on flavonoid chemodiversity. Front Plant Sci 10:821. https://doi.org/10.3389/fpls.2019.00821
- Ververidis F, Trantas E, Douglas C, Vollmer G, Kretzschmar G, Panopoulos N (2007) Biotechnology of flavonoids and other phenylpropanoid-derived natural products. Part I: chemical diversity,

impacts on plant biology and human health. Biotechnol J 2:1214– 1234. https://doi.org/10.1002/biot.200700084

- Sudheeran PK, Ovadia R, Galsarker O, Maoz I, Sela N, Maurer D, Feygenberg O, Oren Shamir M, Alkan N (2020) Glycosylated flavonoids: fruit's concealed antifungal arsenal. New Phytol 225:1788–1798. https://doi.org/10.1111/nph.16251
- Rudall PJ (2020) Colorful cones: how did flower color first evolve? J Exp Bot 71:759–767. https://doi.org/10.1093/jxb/erz479
- Shi MZ, Xie DY (2014) Biosynthesis and metabolic engineering of anthocyanins in *Arabidopsis thaliana*. Recent Pat Biotechnol 8:47–60. https://doi.org/10.2174/1872208307666131218123538
- Jiang H, Yang L, Ma GX, Xing XD, Yan ML, Zhang YY, Wang QH, Yang BY, Kuang HX, Xu XD (2017) New phenylpropanoid derivatives from the fruits of *Xanthium sibiricum* and their antiinflammatory activity. Fitoterapia 117:11–15. https://doi.org/10. 1016/j.fitote.2016.12.007
- Wan H, Yu C, Han Y, Guo X, Luo L, Pan H, Zheng T, Wang J, Cheng T, Zhang Q (2019) Determination of flavonoids and carotenoids and their contributions to various colors of rose cultivars (*Rosa* spp.). Front Plant Sci 10:123. https://doi.org/10.3389/fpls. 2019.00123
- Peng M, Shahzad R, Gul A, Subthain H, Shen S, Lei L, Zheng Z, Zhou J, Lu D, Wang S, Nishawy E, Liu X, Tohge T, Fernie AR, Luo J (2017) Differentially evolved glucosyltransferases determine natural variation of rice flavone accumulation and UV-tolerance. Nat Commun 8:1975. https://doi.org/10.1038/s41467-017-02168-x
- Grunewald S, Marillonnet S, Hause G, Haferkamp I, Neuhaus HE, Ve
 β A, Hollemann T, Vogt T (2020) The tapetal major facilitator NPF2.8 is required for accumulation of flavonol glycosides on the pollen surface in *Arabidopsis thaliana*. Plant Cell 32:1727–1748. https://doi.org/10.1105/tpc.19.00801
- Dastmalchi M, Dhaubhadel S (2015) Proteomic insights into synthesis of isoflavonoids in soybean seeds. Proteomics 15:1646– 1657. https://doi.org/10.1002/pmic.201400444
- Dong NQ, Lin HX (2021) Contribution of phenylpropanoid metabolism to plant development and plant–environment interactions. J Integr Plant Biol 63:180–209. https://doi.org/10.1111/ jipb.13054
- Chen S, Wu F, Li Y, Qian Y, Pan X, Li F, Wang Y, Wu Z, Fu C, Lin H, Yang A (2019) NtMYB4 and NtCHS1 are critical factors in the regulation of flavonoid biosynthesis and are involved in salinity responsiveness. Front Plant Sci 10:178. https://doi.org/ 10.3389/fpls.2019.00178
- Yildiztugay E, Ozfidan-Konakci C, Kucukoduk M, Turkan I (2020) Flavonoid naringenin alleviates short-term osmotic and salinity stresses through regulating photosynthetic machinery and chloroplastic antioxidant metabolism in *Phaseolus vulgaris*. Front Plant Sci 11:682. https://doi.org/10.3389/fpls.2020.00682
- Hapeshi A, Benarroch JM, Clarke DJ, Waterfield NR (2019) Iso-propyl stilbene: a life cycle signal? Microbiology (Read) 165:516–526
- 26. Huang DD, Shi G, Jiang Y, Yao C, Zhu C (2020) A review on the potential of Resveratrol in prevention and therapy of diabetes and diabetic complications. Biomed Pharmacother 125:109767
- Pan MH, Wu JC, Ho CT, Lai CS (2018) Antiobesity molecular mechanisms of action: resveratrol and pterostilbene. BioFactors 44:50–60
- Banik K, Ranaware AM, Harsha C, Nitesh T, Girisa S, Deshpande V, Kunnumakkara AB (2020) Piceatannol: a natural stilbene for the prevention and treatment of cancer. Pharmacol Res 153:104635
- Mattio LM, Catinella G, Pinto A, Dallavalle S (2020) Natural and nature-inspired stilbenoids as antiviral agents. Eur J Med Chem 202:112541

- Tian B, Liu J (2019) Resveratrol: a review of plant sources, synthesis, stability, modification and food application. J Sci Food Agric 100:1392–1404
- Teka T, Zhang L, Ge X, Li Y, Han L, Yan X (2022) Stilbenes: source plants, chemistry, biosynthesis, pharmacology, application and problems related to their clinical application—a comprehensive review. Phytochemistry 197:113128
- Keylor MH, Matsuura BS, Stephenson CR (2015) Chemistry and biology of resveratrol-derived natural products. Chem Rev 115:8976–9027. https://doi.org/10.1021/cr500689b
- Blaszczyk A, Sady S, Sielicka-Rózyńska M (2019) The stilbene profile in edible berries. Phytochem Rev 18:37–67. https://doi.org/ 10.1007/s11101-018-9580-2
- Matos MJ, Santana L, Uriarte EA, Abreu O, Molina E, Yordi EG (2015) Coumarins—an important class of phytochemicals. In: Rao AV, Rao LG (eds) Phytochemicals-isolation, characterisation and role in human health. IntechOpen. https://doi.org/10.5772/59982
- Robe K, Izquierdo E, Vignols F, Rouached H, Dubos C (2021) The coumarins: secondary metabolites playing a primary role in plant nutrition and health. Trends Plant Sci 26:248–259. https:// doi.org/10.1016/j.tplants.2020.10.008
- Stringlis IA, de Jonge R, Pieterse CMJ (2019) The age of coumarins in plant-microbe interactions. Plant Cell Physiol 60:1405–1419. https://doi.org/10.1093/pcp/pcz076
- Jin CW, You GY, He YF, Tang C, Wu P, Zheng SJ (2007) Iron deficiency-induced secretion of phenolics facilitates the reutilization of root apoplastic iron in red clover. Plant Physiol 144:278– 285. https://doi.org/10.1104/pp.107.095794
- Stassen MJJ, Hsu SH, Pieterse CMJ, Stringlis IA (2021) Coumarin communication along the microbiome-root-shoot axis. Trends Plant Sci 26:169–183. https://doi.org/10.1016/j.tplants.2020.09. 008
- Verbon EH, Trapet PL, Stringlis IA, Kruijs S, Pieterse BPAHM (2017) Iron and immunity. Annu Rev Phytopathol 55:355–375. https://doi.org/10.1146/annurev-phyto-080516-035537
- 40. Yang L, Ding W, Xu Y, Wu D, Li S, Chen J, Guo B (2016) New insights into the antibacterial activity of hydroxycoumarins against *Ralstonia solanacearum*. Molecules 21:468. https://doi. org/10.3390/molecules21040468
- 41. Schenke D, Bottcher C, Scheel D (2011) Crosstalk between abiotic ultraviolet-B stress and biotic (flg22) stress signalling in Arabidopsis prevents flavonol accumulation in favor of pathogen defense compound production. Plant Cell Environ 34:1849–1864. https://doi.org/10.1111/j.1365-3040.2011.02381.x
- Pastirova A, Repcak M, Eliasova A (2004) Salicylic acid induces changes of coumarin metabolites in *Matricaria chamomilla* L. Plant Sci 167:819–824. https://doi.org/10.1016/j.plantsci.2004. 05.027
- Zhao SS, Li S, Luo ZH, Zhou ZQ, Li N, Wang Y, Yao XS, Gao H (2021) Bioactive phenylpropanoid derivatives from the fruits of *Lycium ruthenicum* Murr. Bioorg Chem 116:105307. https://doi. org/10.1016/j.bioorg.2021.105307
- Labeeuw L, Martone PT, Boucher Y, Case RJ (2015) Ancient origin of the biosynthesis of lignin precursors. Biol Direct 10:23. https://doi.org/10.1186/s13062-015-0052-y
- Wang Y, Chantreau M, Sibout R, Hawkins S (2013) Plant cell wall lignification and monolignol metabolism. Front Plant Sci 4:220. https://doi.org/10.3389/fpls.2013.00220
- Heleno SA, Martins A, Queiroz MJ, Ferreira IC (2015) Bioactivity of phenolic acids: metabolites versus parent compounds: a review. Food Chem 173:501–513. https://doi.org/10.1016/j.foodc hem.2014.10.057
- Widhalm JR, Dudareva N (2015) A familiar ring to it: biosynthesis of plant benzoic acids. Mol Plant 8:83–97. https://doi.org/ 10.1016/j.molp.2014.12.001

 Rana S, Bhushan S (2016) Apple phenolics as nutraceuticals: assessment, analysis and application. J Food Sci Technol 53:1727–1738. https://doi.org/10.1007/s13197-015-2093-8

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

- Bhattacharya A, Sood P, Citovsky V (2010) The roles of plant phenolics in defense and communication during Agrobacterium and Rhizobium infection. Mol Plant Pathol 11:705–719. https:// doi.org/10.1111/j.1364-3703.2010.00625.x
- 51. Xue JS, Zhang B, Zhan H, Lv Y-L, Jia X-L, Wang T, Yang N-Y, Lou Y-X, Zhang Z-B, Hu W-J, Gui J, Cao J, Xu P, Zhou Y, Hu J-F, Li L, Yang Z-N (2020) Phenylpropanoid derivatives are essential components of sporopollenin in vascular plants. Mol Plant 13:1644–1653. https://doi.org/10.1016/j.molp.2020.08. 005
- Cuendet M, Potterat O, Hostettmann K (2001) Flavonoids and phenylpropanoid derivatives from *Campanula barbata*. Phytochemistry 56:631–636. https://doi.org/10.1016/s0031-9422(00) 00423-4
- Jiang N, Doseff AI, Grotewold E (2016) Flavones: from biosynthesis to health benefits. Plants (Basel) 5:27. https://doi.org/10. 3390/plants5020027
- 54. Guo R, Shang XY, Lv TM, Yao GD, Lin B, Wang XB, Huang XX, Song SJ (2019) Phenylpropanoid derivatives from the fruit of *Crataegus pinnatifida* Bunge and their distinctive effects on human hepatoma cells. Phytochemistry 164:252–261. https://doi.org/10.1016/j.phytochem.2019.05.005
- 55. Ma Q, Wei R, Yang M, Huang X, Zhong G, Sang Z, Dong J, Shu J, Liu J, Zhang R, Yang J, Wang A, Ji T, Su Y (2019) Structures and biological evaluation of phenylpropanoid derivatives from *Murraya koenigii*. Bioorg Chem 86:159–165. https://doi.org/10.1016/j.bioorg.2019.01.038
- 56. Xia Z, Xu TQ, Zhang HX, Chen YM, Zhou GX (2022) New phenylpropanoids from the fruits of *Xanthium sibiricum* and their anti-inflammatory activity. Nat Prod Res 36:805–813. https://doi.org/10.1080/14786419.2020.1806273
- Ramaroson ML, Koutouan C, Helesbeux JJ, Le Clerc V, Hamama L, Geoffriau E, Briard M (2022) Role of phenylpropanoids and flavonoids in plant resistance to pests and diseases. Molecules 27:8371. https://doi.org/10.3390/molecules27238371
- Yadav V, Wang Z, Wei C, Amo A, Ahmed B, Yang X, Zhang X (2020) Phenylpropanoid pathway engineering: an emerging approach towards plant defense. Pathogens 9:312. https://doi. org/10.3390/pathogens9040312
- Sharma A, Shahzad B, Rehman A, Bhardwaj R, Landi M, Zheng B (2019) Response of phenylpropanoid pathway and the role of polyphenols in plants under abiotic stress. Molecules 24:2452. https://doi.org/10.3390/molecules24132452
- 60. Chen S, Wang Q, Lu H, Li J, Yang D, Liu J, Yan C (2019) Phenolic metabolism and related heavy metal tolerance mechanism in *Kandelia obovata* under Cd and Zn stress. Ecotoxicol Environ Saf 169:134–143. https://doi.org/10.1016/j.ecoenv.2018.11.004
- 61. Nichols SN, Hofmann RW, Williams WM (2015) Physiological drought resistance and accumulation of leaf phenolics in white clover interspecific hybrids. Environ Exp Bot 119:40–47. https://doi.org/10.1016/j.envexpbot.2015.05.014
- Bistgani ZE, Hashemi M, DaCosta M, Craker L, Maggi F, Morshedloo MR (2019) Effect of salinity stress on the physiological characteristics, phenolic compounds and antioxidant activity of *Thymus vulgaris* L. and *Thymus daenensis* Celak. Ind Crops Prod 135:311–320. https://doi.org/10.1016/j.indcrop.2019.04.055
- Agati G, Tattini M (2010) Multiple functional roles of flavonoids in photoprotection. New Phytol 186:786–793. https://doi.org/10. 1111/j.1469-8137.2010.03269.x

- Singh P, Singh A, Choudhary KK (2023) Revisiting the role of phenylpropanoids in plant defense against UV-B stress. Plant Stress 7:100153. https://doi.org/10.1016/j.stress.2023.100143
- Commisso M, Toali K, Strazzer P, Stocchero M, Ceoldo S, Baldan B, Levi M, Guzzo F (2016) Impact of phenylpropanoid compounds on heat stress tolerance in carrot cell cultures. Front Plant Sci 7:1439. https://doi.org/10.3389/fpls.2016.01439
- Mahdavi V, Farimani MM, Fathi F, Ghassempour A (2015) A targeted metabolomics approach toward understanding metabolic variations in rice under pesticide stress. Anal Biochem 478:65–72. https://doi.org/10.1016/j.ab.2015.02.021
- Neelam K, Duddu V, Anyim N, Neelam J, Lewis S (2021) Pandemics and pre-existing mental illness: a systematic review and meta-analysis. Brain Behav Immun Health 10:100177. https://doi. org/10.1016/j.bbih.2020.100177
- 68. Yang W, Xu X, Li Y, Wang Y, Li M, Wang Y, Ding X, Chu Z (2016) Rutin-mediated priming of plant resistance to three bacterial pathogens initiating the early SA signal pathway. PLoS ONE 11:e0146910. https://doi.org/10.1371/journal.pone.0146910
- 69. Szatmári Á, Zvara Á, Móricz ÁM, Besenyei E, Szabó E, Ott PG, Puskás LG, Bozsó Z (2014) Pattern triggered immunity (PTI) in tobacco: isolation of activated genes suggests role of the phenylpropanoid pathway in inhibition of bacterial pathogens. PLoS ONE 9:e102869. https://doi.org/10.1371/journal.pone.0102869
- Hijaz FM, Manthey JA, Folimonova SY, Davis CL, Jones SE, Reyes-De-Corcuera JI (2013) An HPLC-MS characterization of the changes in sweet orange leaf metabolite profile following infection by the bacterial pathogen *Candidatus liberibacter asiaticus*. PLoS ONE 8:e79485. https://doi.org/10.1371/journal. pone.0079485
- Koutouan C, Clerc VL, Baltenweck R, Claudel P, Halter D, Hugueney P, Hamama L, Suel A, Huet S, Merlet MHB, Briard M (2018) Link between carrot leaf secondary metabolites and resistance to *Alternaria dauci*. Sci Rep 8:13746. https://doi.org/ 10.1038/s41598-018-31700-2
- 72. Kröner A, Marnet N, Andrivon D, Val F (2012) Nicotiflorin, rutin and chlorogenic acid: phenylpropanoids involved differently in quantitative resistance of potato tubers to biotrophic and necrotrophic pathogens. Plant Physiol Biochem 57:23–31. https://doi. org/10.1016/j.plaphy.2012.05.006
- Krcatović E, Rusak G, Bezić N, Krajacić M (2008) Inhibition of tobacco mosaic virus infection by quercetin and vitexin. Acta Virol 52:119–124
- Tagousop CN, Tamokou JDD, Ekom SE, Ngnokam D, Voutquenne-Nazabadioko L (2018) Antimicrobial activities of flavonoid glycosides from *Graptophyllum grandulosum* and their mechanism of antibacterial action. BMC Complement Altern Med 18:252. https://doi.org/10.1186/s12906-018-2321-7
- Farhadi F, Khameneh B, Iranshahi M, Iranshahy M (2019) Antibacterial activity of flavonoids and their structure–activity relationship: an update review. Phyther Res 33:13–40. https://doi.org/ 10.1002/ptr.6208
- 76. Wang LH, Zeng XA, Wang MS, Brennan CS, Gong D (2018) Modification of membrane properties and fatty acids biosynthesis-related genes in *Escherichia coli* and *Staphylococcus aureus*: implications for the antibacterial mechanism of naringenin. Biochim Biophys Acta Biomembr 1860:481–490. https://doi.org/10. 1016/j.bbamem.2017.11.007
- 77. MacDonald MC, Arivalagan P, Barre DE, MacInnis JA, D'Cunha GB (2016) *Rhodotorula glutinis* phenylalanine/tyrosine ammonia lyase enzyme catalyzed synthesis of the methyl ester of parahydroxycinnamic acid and its potential antibacterial activity. Front Microbiol 7:281. https://doi.org/10.3389/fmicb.2016.00281
- 78. Cheah H-L, Lim V, Sandai D (2014) Inhibitors of the glyoxylate cycle enzyme ICL1 in *Candida albicans* for potential use as

antifungal agents. PLoS ONE 9:e95951. https://doi.org/10.1371/ journal.pone.0095951

- Xie Y, Huang B, Yu K, Shi F, Liu T, Xu W (2013) Caffeic acid derivatives: a new type of influenza neuraminidase inhibitors. Bioorg Med Chem Lett 23:3556–3560. https://doi.org/10.1016/j. bmcl.2013.04.033
- Hariono M, Abdullah N, Damodaran KV, Kamarulzaman EE, Mohamed N, Hassan SS, Shamsuddin S, Wahab HA (2016) Potential new H1N1 neuraminidase inhibitors from ferulic acid and vanillin: molecular modelling, synthesis and in vitro assay. Sci Rep 6:38692. https://doi.org/10.1038/srep38692
- Amano R, Yamashita A, Kasai H, Hori T, Miyasato S, Saito S, Yokoe H, Takahashi K, Tanaka T, Otoguro T (2017) Cinnamic acid derivatives inhibit hepatitis C virus replication via the induction of oxidative stress. Antiviral Res 145:123–130. https://doi. org/10.1016/j.antiviral.2017.07.018
- Wu Z-M, Yu Z-J, Cui Z-Q, Peng L-Y, Li H-R, Zhang C-L, Shen H-Q, Yi P-F, Fu B-D (2017) In vitro antiviral efficacy of caffeic acid against canine distemper virus. Microb Pathog 110:240–244. https://doi.org/10.1016/j.micpath.2017.07.006
- Rempe CS, Burris KP, Lenaghan SC, Stewart CN (2017) The potential of systems biology to discover antibacterial mechanisms of plant phenolics. Front Microbiol 8:422. https://doi.org/10.3389/ fmicb.2017.00422
- Borges A, Saavedra MJ, Simões M (2015) Insights on antimicrobial resistance, biofilms and the use of phytochemicals as new antimicrobial agents. Curr Med Chem 22:2590–2614. https://doi. org/10.2174/0929867322666150530210522
- Kumazawa S, Kajiya K, Naito A, Saito H, Tuzi S, Tanio M, Suzuki M, Nanjo F, Suzuki E, Nakayama T (2004) Direct evidence of interaction of a green tea polyphenol, epigallocatechin

gallate, with lipid bilayers by solid-state nuclear magnetic resonance. Biosci Biotechnol Biochem 68:1743–1747. https://doi.org/ 10.1271/bbb.68.1743

- 86. Zhang L, Kong Y, Wu D, Zhang H, Wu J, Chen J, Ding J, Hu L, Jiang H, Shen X (2008) Three flavonoids targeting the β-hydroxyacyl-acyl carrier protein dehydratase from *Helicobacter pylori*: crystal structure characterization with enzymatic inhibition assay. Protein Sci 17:1971–1978. https://doi.org/10.1110/ps. 036186.108
- Shakya T, Stogios PJ, Waglechner N, Evdokimova E, Ejim L, Blanchard JE, McArthur AG, Savchenko A, Wright GD (2011) A small molecule discrimination map of the antibiotic resistance kinome. Chem Biol 18:1591–1601. https://doi.org/10.1016/j. chembiol.2011.10.018
- Hemaiswarya S, Doble M (2010) Synergistic interaction of phenylpropanoids with antibiotics against bacteria. J Med Microbiol 59:1469–1476. https://doi.org/10.1099/jmm.0.022426-0
- Oh E, Jeon B (2015) Synergistic anti-*Campylobacter jejuni* activity of fluoroquinolone and macrolide antibiotics with phenolic compounds. Front Microbiol 6:1129. https://doi.org/10.3389/ fmicb.2015.01129

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