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Flavonoids in Agriculture

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Abstract

Flavonoids are compounds that are secondary metabolites, but which play an important role in the biological activities of plants. They can be responsible for the color of flowers and fruits and for the attraction of pollinators. They also participate in plant-microorganism symbiosis. These relationships can be used to naturally control weeds and insect pests and reduce stress and diseases in order to increase crop yield. To improve the understanding of the different biological systems where flavonoids are involved in their symbiotic relationships and in plant physiology, tools such as metabolomics are used, which give a broader picture and allow to search for strategies to solve problems specific to the agricultural sector.

Keywords: flavonoids, agriculture, plants, metabolomics

1. Introduction

Flavonoids are secondary metabolites of plants; this group of phenolic compounds includes approximately 4500 compounds [1]. They are classified into different subgroups (**Figure 1**). Their nuclear structure includes carbons C6-C3-C6, and the diversity of flavonoids depends on the position of the aromatic ring [2].

Flavonoids and flavones are the most common in plants, whereas flavanones, flavanols, dihydroflavones, and dihydrochalcones have a limited distribution. Flavonoids are present in plant tissues in relatively high concentrations in free forms (aglycones) or conjugated with sugar molecules (glycosides) [5].

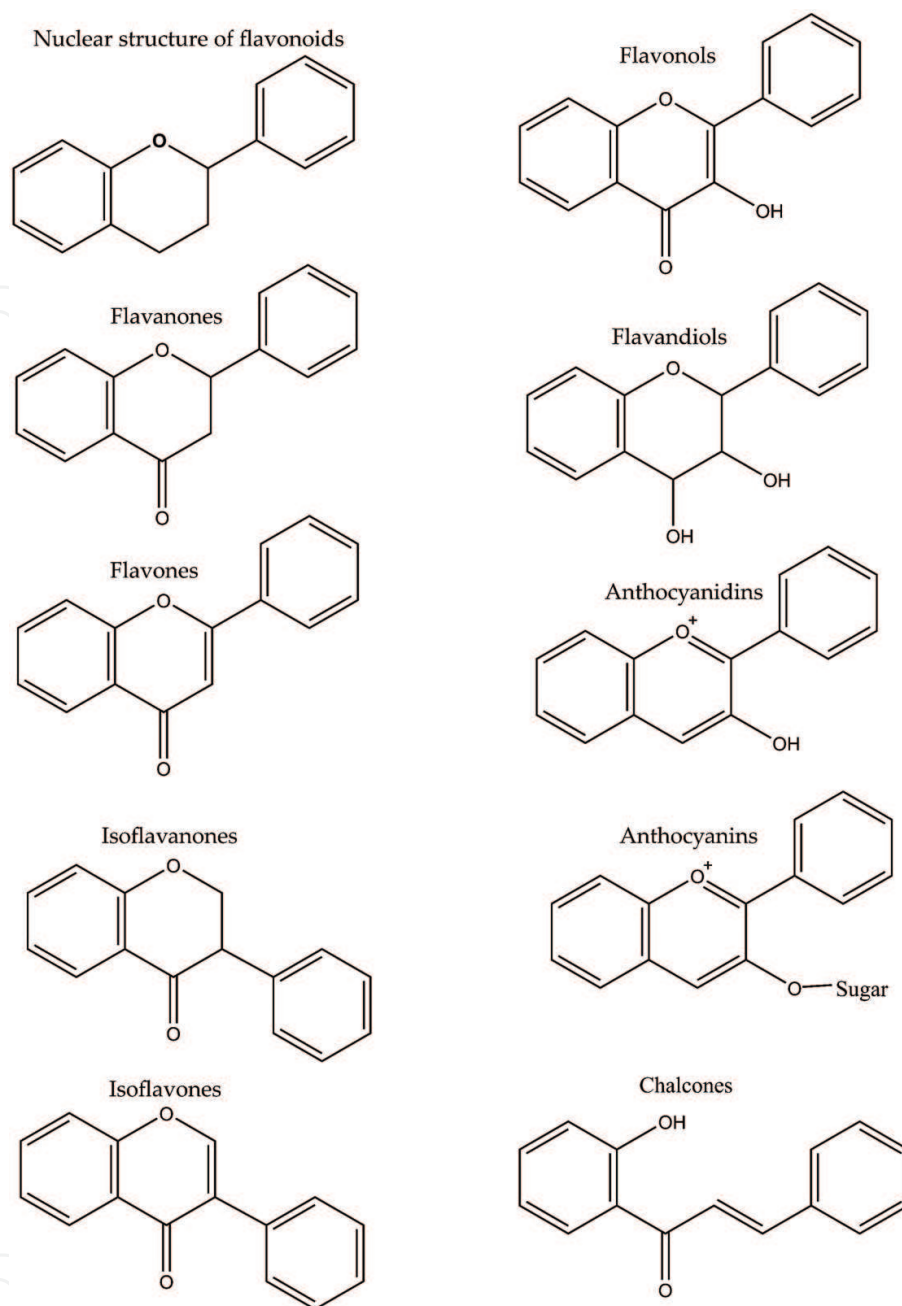


Figure 1. Structure of the different types of flavonoids (modified from Refs. [3, 4]).

Flavonoids are polyphenolic compounds found in all vascular and non-vascular plants [6]. They are important in the diet of humans because they possess a high nutritional value; besides, they are used as effective medicines in the treatments of certain diseases, and therefore, they are called nutraceuticals. Nowadays, a diet rich in fruits and vegetables is recommended to contribute to the prevention and treatment of cardiovascular diseases, diabetes, cancer, chronic inflammatory disorders, and degenerative diseases [7].

Some examples of nutraceutical flavonoids are the following: isoflavones (genistein, daidzein) obtained from celery, soybeans, and other legumes. Isoflavones have antitumor, anticancer,

and antioxidant action, and they improve immune response, lower cardiovascular risk, and menopausal symptoms. Quercetin is contained in onion, citrus fruits, broccoli, red grapes, apple, and cherries. Kaempferol is present in broccoli and radishes [8]. Anthocyanins are present in red wine and fruits. These flavonoids are important due to their antioxidant, anticancer, and antithrombotic properties, as well as their ability to lower blood cholesterol [9].

Their concentration can vary among species: in fruits, vegetables, and medicinal plants, ranges from 0 to 6125.6 mg kg⁻¹ have been reported. For example, 1720.5 mg kg⁻¹ has been observed in spinach, 3575.4 mg kg⁻¹ in strawberry, and 459.9 mg kg⁻¹ in apple [10].

2. Function of flavonoids in plants

In plants, flavonoids play important roles in many biological processes (**Figure 2**). They participate in seed development and growth [11], fruit growth and ripening [12], pollen tube germination [13], and hormone transport [6]. Flavonoids respond to biotic and abiotic factors by providing antioxidant properties; they prevent damage caused by fungi, viruses, bacteria, and herbivores; function as chemical messengers in association with mycorrhizae and bacteria; act as chemical attractants to pollinating animals; and have allelopathic functions [14, 15].

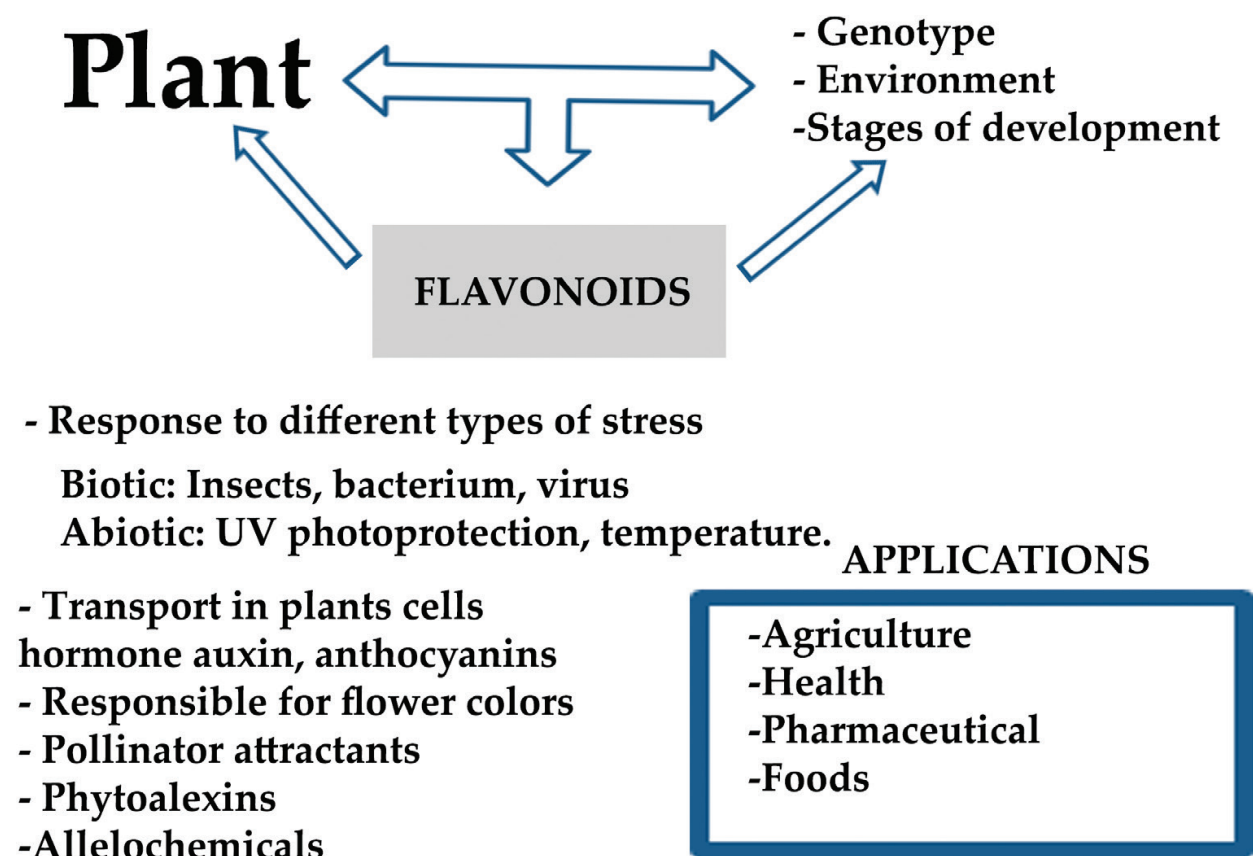


Figure 2. Main functions of flavonoids in plants (modified from Refs. [17–19]).

They also participate in pigment and color differences in flowers, fruits, and seeds [3]. For example, flavonols are related with yellow, flavanols with ochre to brown, and anthocyanins with red to purple [4]. In the case of corn kernels and petunia flowers, anthocyanins and proanthocyanidins are mainly responsible for the pigments. These accumulate in the vacuole or cell wall. In corn, accumulation occurs by vacuolar sequestration of anthocyanins [16].

As part of their defense strategy, plants induce systems of antioxidant activity, reactive oxygen species (ROS), enzymatic and non-enzymatic, soluble in water and in lipids, located in different cell compartments. The enzymatic ROS system consists of several enzymes such as superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APX), monodehydroascorbate reductase (MDAR), dehydroascorbate reductase (DHAR), glutathione peroxidase (GPX), and glutathione reductase (GR). Non-enzymatic antioxidants include pigments (carotenoids, anthocyanidins), vitamins (A, C, E), and flavonoids, among others [19]. The synthesis of the latter compounds by the plants is related to environmental biotic and abiotic stress factors. Plants subjected to conditions of severe stress accumulate dihydroxy B-ring substituted flavonoids, which are effective eliminators of ROS.

Flavonoids activate a network of events, including stress-induced morphogenesis, which protects plants from unexpected lesions of different origins [15]. Therefore, flavonoids play an important role in the protection of biological systems against the harmful effects of oxidative processes on macromolecules, they are important to catalyze electron transport and to eliminate reactive oxygen, especially in the form of superoxide anions, hydroxyl radicals, lipid peroxides, or hydroperoxides. In this way, they block the deleterious activity of these substances on the cells [15, 20].

3. Flavonoids: allelopathy and its applications in agriculture

Allelopathy is defined as the direct or indirect effect of secondary compounds produced by a donor plant on a recipient plant. This type of relationship can be beneficial or harmful [21].

Currently, to solve multiple problems in agriculture, allelopathy is being considered as a natural control of weeds and insect pests and to reduce stress and diseases, in order to increase crop yield [22, 23]. Weeds are the species that compete the most with crops, and for their management, aqueous extracts are used, such as natural herbicides from sorghum, sunflower, eucalyptus, and rice, among others; a greater efficacy is obtained when they are mixed together than alone [24]. On the other hand, it has been demonstrated that exudates of roots of rice plants reduce the attack of fungi of the genus *Fusarium* in melon. In addition, plants of *Brassica napus* L., incorporated into the soil, decrease the population of certain nematodes in orchards [23]. These examples show the potential of some allelochemicals to generate herbicides, fungicides, insecticides, and nematicides.

Knowledge of allelopathy can be valuable to improve crop rotation proposals [22]. Recent publications highlight the role of flavonoids in allelopathy, involved in soil interactions, since they have been identified in significant concentrations in many bioactive root exudates. Simple phenols and flavonoids are released by the decomposition of plant tissues as leachates and by the process of microbial degradation and transformation in the soil [22, 24].

In many legumes, it has been shown that the flavonoids quercetin and kaempferol, free and glycosylated, commonly released by germinating seeds and roots, persist for days in the soil and possess an important phytoinhibitory activity, stimulating seed germination at low concentrations but inhibiting seedling growth at high concentrations. These compounds are also present in leaf extracts of walnut trees [25].

The activity of several flavonoids is highly concentration-dependent; some of these compounds may be inhibitory or stimulatory, depending on the availability of the concentration in the soil/water solution in the rhizosphere [21]. Other allelopathic flavonoids are luteonarin, saponarin, and isovitexin, as well as catechin and cyanidin, luteolin 7-O- β -glucuronide, neochamaejasmin, mesoneochamaejasmin, chamaejasmenin, genkwanol, daphnodorin, and dihydrodaphnodorin, among others [21, 26, 27]. Allelochemicals directly and indirectly affect plants; indirect effects include soil alteration, physicochemical properties, changes in microbial populations, and differential nutrient availability for plants. The direct action is the physiological and biochemical changes generated during plant growth and development [22, 28]. Scientific studies have demonstrated several mechanisms of action of flavonoids when applied exogenously on plants. Such as changes in membrane permeability and inhibition of plant nutrient absorption, inhibition of cell division, elongation and submicroscopic structure, effects on photosynthesis and respiration of the plant, consequences on different enzymatic functions and activities, effects on the synthesis of endogenous hormones and proteins, and the disruption of adenosine triphosphate (ATP) formation [28].

4. Metabolomics: flavonoids as a tool in agriculture

It has been described that over 7000 natural products belong to the flavonoid family and to analyze them, physicochemical methods as nuclear magnetic resonance (NMR) and mass spectrometry have been used [29], but nowadays the most important issue is concerned with the identification of free and conjugated forms of these compounds. Metabolite profiling is an essential tool to analyze the effects of pathway engineering approaches; in this sense, the metabolomics approach used to solve this problem as the liquid-chromatography-mass spectrometry has supported the quantitative and qualitative analysis of flavonoids. In addition, straightforward and efficient methods approach toward rapid flavonoid identification by combining simple high-performance liquid chromatography (HPLC) and NMR methods, facilitating the analysis of flavones and flavanones [30].

The literature describes a lot of information on metabolomics in areas of medicinal plants, chemosystematics, adulteration of plants, and so on, but it is scarce in agriculture [31]. Flavonoids are a diverse group in agricultural crops, and there are studies using metabolomic tools to analyze the content of flavonoids using different analytical techniques (**Table 1**).

Red tomato contains flavonoids mainly in the peel; through omic studies, it may be possible to modify the pattern of flavonoids in the pulp [42]. Metabolic profiling represents a useful tool to characterize varieties with functional markers, such as flavonoids. For example, metabolite profiling allowed the characterization of Italian tomato landraces and different fruit types [43].

| Crop | Plant organs | Analytical technique | Compound | Reference |
|------------------------------------|---------------|--|--|-----------|
| Soybean | Leaves | (RP)-HPLC and ¹ H NMR | Naringenin, rutin, quercetin, kaempferol and its glucosides, and total flavonoids | [32] |
| Red tomato | Fruit | HPLC/DAD and LC/NMR, LC/MS, and LC/MS/MS | Naringenin chalcone and rutin | [33] |
| Red and yellow raspberry cultivars | Fruit | UPLC/QqQ-MS/MS | Flavan-3-ol, quercetin-3,4-diglucoside, quercetin, kaempferol-3-glucuronide, rutin, and the conjugates of isorhamnetin | [34] |
| Avocado | Fruit | MS/MS LC-DAD-ESI-TOF MS | Catechin and epicatechin Rutin, Naringin, kaempferol, apigenin, luteolin, isorhamnetin | [35] |
| Maize | Kernels | LC-MS/MS | Apigenin, luteolin, methyl chrysoeriol, malvidin, pentose, rhamnose, selgin, tricin, chalcone synthase, chalcone isomerase | [36] |
| Rice | Leaf and bran | LC-QTOF-MS | Tricin, tricin 7-O-rutinoside, and tricin 7-O-β-D-glucopyranoside | [37] |
| Wheat | Flag leaf | UPLC-QTOF MS/MS | Isovitexin, isoorientin, Isoschaftoside, quercetin 3-rutinoside-7-glucoside and methylisoorientin-2"-O-rhamnoside | [38] |
| Grape | Berries | LC-MS | Quercetin and derivatives, kaempferol and isorhamnetin | [39] |
| Broad bean | Pods | UHPLC-ESI-qTOF-MS ² | Glycosylated flavonoids | [40] |
| Tea | Leaves | UPLC-Q-TOF MS | Flavan-3-ols, flavonols and their glucosides | [41] |

Table 1. Metabolomic studies of flavonoids in agricultural crops.

Another study related with metabolomic profiling is the analysis of flavonoid distribution in three *Momordica* species, where 13 flavonoids were found in a special pattern [44].

The novel approach of genetic metabolomics referred to as metabolite profiling combined with quantitative trait locus (QTL) analysis was applied to detect flux control points in flavonoids biosynthesis of *Populus*. It was found that flavonoid profile can be used for QTL analysis to reveal loci that control the flux of their biosynthesis [45].

Plant metabolism is disrupted by several types of stress. Flavonoids are involved in the response toward abiotic stress [46]; a good model to understand how flavonoids contribute to the mitigation of oxidative and drought stress is *Arabidopsis thaliana*. Another example is the metabolomic analysis of tea, where the effects of light intensity and temperature on the metabolites in tea grown in the shade were evaluated; they found that most flavonoids (flavan-3-ols, flavonols, and their glucosides) decreased significantly in the shading treatments. Their study also showed a greater effect of temperature on galloylation of catechins than light intensity [41].

The growing stage of plants has been studied in connection with flavonoid synthesis, an interesting metabolomic study is the analysis of soybean leaves [47], it showed significant changes in the content of flavonoids and isoflavonoids, and kaempferol derivatives were used

as markers. The results demonstrated that metabolite production changed depending on the growing stage, and they mention that the information can be useful to understand physiological characterization and suggest an optimal harvesting time of this crop.

Metabolic analysis has the potential to generate a complete vision of metabolic networks and has revealed multiple detection, quantification, and analysis strategies to evaluate numerous metabolites such as flavonoids. This tool attempts to integrate compound and metabolite analyses along with other biological data overview of plants, for example, phenotypic, morphological, and genetic data [48].

5. Symbiosis flavonoids-microorganisms

Flavonoids are considered signaling compounds in plant-microorganisms symbiosis; their function is signaling in response to pathogens, bacteria, fungi. Their participation is important in the nodulation of roots, where they are secreted to the rhizosphere [21], in the case of legumes under low nitrogen conditions, and where their interaction is specific with gram-negative bacteria called rhizobia that are nitrogen fixers [49]. They are also involved in the transcription of genes for the biosynthesis of rhizobial signaling molecules called Nod factors, which are perceived by the plant to allow symbiotic root infection [49]. Therefore, they can stimulate or inhibit rhizobial Nod gene expression. Root exudates can be flavonoids that participate as signaling compounds in the arbuscular mycorrhizal symbiosis [50]. Root exudation of flavonoids increases or decreases depending on the response to the symbiotic and pathogenic interaction of the plant and microbes.

It has been shown that certain flavonoids are stimulants for the germination of ectomycorrhizal fungi spores [50]. Depending on the arbuscular mycorrhizal fungi colonizers of the roots and the stage of symbiosis development [51].

The flavonoid role in the rhizosphere (**Table 2**) is important in agriculture because flavonoid interaction in the symbiosis with microorganisms can be a tool for nitrogen fixation in soils

| Participation | Flavonoid | Species | Symbiosis type | Cite |
|---|---|-------------------------------------|----------------|------|
| Stimulant for germination of spores | Coumestrol, medicarpin, ononin, formononetin, daidzein, genistein, biochanin A and 4',7-dihydroxyflavanone, 4,4'-dihydroxy-2'-methoxychalcone | <i>Medicago sativa</i> L. cv. Sitel | Fungus | [51] |
| | hesperidin, morin, rutin, quercetin, naringenin, genistein, and chrysin | <i>Suillus bovinus</i> | Fungus | [52] |
| Chemo attractant response from the rhizobia | Luteolin and apigenin | – | Bacterium | [53] |
| Auxin transport inhibitors | Kaempferol | <i>Medicago truncatula</i> | – | [54] |

Table 2. Role of flavonoids in the rhizosphere.

poor in macronutrients. It can be a strategy to stimulate beneficial bacteria or inhibit harmful bacteria and fungi. It can also be considered in the genetic improvement of plant species.

6. Importance of flavonoids in pest control

Every day, the demand for natural products obtained from plants increases to be used as pest control agents. New pesticides are being developed using flavonoids, as they are an alternative to synthetic pesticides. They can inhibit enzymatic activity and prevent the growth of larvae of different insect species [55]. Some flavonoids interfere in the process of moulting and reproduction of several insects, that is, they inhibit the formation of juvenile hormone (ecdysone). Flavonoids inhibit transcription of ecdysone receptor-dependent genes (EcR) [56].

It has been reported that some types of flavonoids have had an effect on agricultural pests with ovicidal effect, oviposition, fecundity, mortality, weight reduction, and emergence of adults [57, 58]. Quercetin, rutin, and naringin showed positive effects for the control of nymphs and adults of the aphid *Eriosoma lanigerum* Hausmann. These can be used as an insecticide in the integrated management programs of this aphid [59]. Some flavonoids can influence agricultural pests depending on the concentration applied; if they are low, they do not affect them [60]; therefore, it is necessary to test the minimum concentrations for the flavonoid to have an insecticidal effect.

7. Concluding remarks

Throughout this chapter, the importance and interest in the knowledge of flavonoids as a big group of natural products, present in different organisms, have been emphasized. They have been widely investigated, from their biosynthesis, analytical techniques for their analysis, to their biological activity. They are compounds with different responses to biotic and abiotic factors, which can influence the agricultural sector as attractants for pollinators, as pigment to flowers and fruits, allelochemical functions, symbiosis with beneficial organisms, and as pest control.

The importance of flavonoids lies not only in the functions in plants but also in different therapeutic and nutraceutical applications. It is a group that is present in a wide variety of plant species, in different concentrations. In addition, its beneficial effects on health have been demonstrated and one of the most notable examples is its antioxidant activity.

However, the information linked to agriculture is scattered. Therefore, the purpose of this chapter is to provide an overview of their applications and show that metabolomics is an effective tool for research linked to metabolic processes of flavonoids with various agricultural crops.

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