|  |
| --- |
| BIOCHEMICAL PATHWAY OF FLAVONOIDS BIOSYNTHESIS |

BIOSYNTHESIS

**ABSTRACT**

Flavonoids are just such a fantastic group of plant compounds! They're polyphenolic, that is to say, they have lots of phenol groups. Such compounds help things like the color of flowers or even foliage that protects against UV rays; these flavonoids might even protect the plant itself from insects. Now let's describe how these flavonoids are biosynthesized. These compounds come from an amino acid called phenylalanine. It's called the phenylpropanoid pathway. It is a recipe that has a series of steps, which form quite an important process! An enzyme called phenylalanine ammonia-lyase, or PAL for short, converts phenylalanine into cinnamic acid.

Then two more enzymes, cinnamate-4-hydroxylase (C4H) & 4-coumarate-CoA ligase (4CL), combine to make p-coumaroyl-CoA. Now things get pretty interesting! The next is the chalcone synthase (CHS) accepts p-coumaroyl-CoA, condenses it with malonyl-CoA, and then chalcones are formed. Chalcone isomerase (CHI) comes afterward and catalyzes chalcone into naringenin. But then the hydroxylation and glycosylation add other cool tweaks that help in the formation of varied flavonoids like quercetin, kaempferol, and anthocyanins. The whole process is very much under tightly-controlled genes and environmental factors; it's something super-important for how plants grow, and could even be good for human health!

1. **INTRODUCTION**

Definition

Flavonoids are a broad group of polyphenolic compounds found in plants and are characterized by having a basic chemical structure consisting of two aromatic rings known as A and B connected by a three-carbon chain, which in turn forms the heterocyclic ring that is always present and designated as C. This central framework can also be substituted by hydroxyl (-OH) groups, methoxy (-OCH₃) groups, and diverse sugar moieties; this gives the level of enormous diversity in subclasses of flavonoids, which consists of flavonols, flavones, isoflavones, flavanones, anthocyanins, and flavanols. Such structural variations have an enormous influence over their biological activities as well as properties.



Fig 1: Classification of Flavonoids

**Classification of Flavonoids**

With the discovery of structures of flavonoids, several classification systems were developed based on their chemical properties. Flavonoids have been broadly categorized into some classes based on their main groups, as follows: Class Flavonols. Compounds that are classified under this category include quercetin and kaempferol, which are commonly found in fruits, vegetables, and tea. They have antioxidant properties.

1. Flavones: Such flavones include apigenin and luteolin. Various herb types contain these compounds, which have been characterized by anti-inflammatory activity.
2. Isoflavones: Mainly occurring in soy, isoflavones like genistein and daidzein are well characterized for their estrogenic activity, and have an important role in studies related to hormone-related conditions.
3. Anthocyanins: These pigments are known to cause a variety of red, purple, and blue colors in fruits and flowers of many. They contain excellent antioxidative properties and health benefits.
4. Flavanones: This category includes compounds such as naringenin and hesperidin. Flavanones are generally found in citrus fruits and have cardiovascular benefits.
5. Flavonolignans: This lesser-known group comprises silybin, which is part of milk thistle and well known for its hepatoprotection.

**Importance of Flavonoids**

* Antioxidant activities: Flavonoids are free radical scavengers that decrease oxidative stress and cellular injury.
* Anti-inflammatory activities: They can alter inflammatory pathways, and this may be an effective way of lowering chronic inflammation.
* Heart Health: Flavonoid consumers also enjoy superior heart health and decreased cardiovascular diseases.
* Anticancer Activities: Some of the flavonoids have been shown to have anticancer activity using inhibiting tumor growth and inducing apoptosis in cancer cells.
* Neuro-protective Effects: Flavonoids can thereby enhance cognitive activities and also help protect against neurodegenerative diseases.
* Anti-microbial Activity: Several flavonoids show anti-microbial activity that will help fight off the pathogens.
* Hormone-level Regulation: Isoflavones seem to act similarly to estrogen and play a supportive role in situations where hormones are involved in the circumstances.
* Dermatoprotection: Flavonoids afford protection to skin against the potent ultraviolet radiation of the sun and also provide fewer chances of developing a disease like skin cancer.
* Gut Health: They provide the safety of maintaining the useful gut microbiota, which contributes to the general health of the digestive system.
* Nutraceutical Value: Flavonoids are used in large amounts in functional foods and dietary supplements with purported health value.

Plant Physiology Functions

* Absorption of UV Light: Flavonoids can absorb UV light to protect the tissues of plants from excessive radiation that may damage them.
* Antioxidant Activities: Flavonoids are scavengers of reactive oxygen species. Thus, they generally protect the plant against oxidative stress created by these damaging reactive oxygen species.
* Attracting Pollinators: Most of these flavonoids contribute towards the coloring of flowers that could attract pollinators.
* Natural pesticide: Flavonoids repel herbivores and inhibit pathogens so could be counted as major roles as natural pesticides.
* Signaling Molecules: They would be involved in the transduction of plant response to environmental stresses and can modulate growth processes.
1. **HISTORICAL BACKGROUND OF FLAVONOID BIOSYNTHESIS**

First study:

The first recorded usage of flavonoids is when scientists began to research the pigments responsible for bright colors in flowers and fruits. Based on the result of the investigation, the survival of plants depends on the most critical tasks that flavonoids function in, rather than aesthetic usages. In the initial experiment, it was discovered that flavonoids are shields against UV radiation for plants and at the same time act as herbal and microbial pests.

As the research advanced, scientists began getting several isolates and characterizations of many flavonoids. This research has, in a manner, broadened the understanding not only of the chemical structure of flavonoids but their biological functions. Work done in this very field by chemists like Edgar Charles B. Hall and other similar chemists has pretty much laid down the foundational understanding of flavonoids; hence, the pathway paving their subsequent detailed further exploration into both plant biology as well as human health applications.

**Evolution of Research in Flavonoid Biosynthesis:**

Research work in flavonoid biosynthesis has, over the years, undergone a series of momentous phases that represent the technological advancement in the related fields of chemistry, molecular biology, and plant sciences.

1. Early Phytochemistry (19th Century)

The early work was basically on the isolation and characterization of the flavonoids coming from different sources of plants. Anthocyanins were identified by Friedrich Wilhelm Runge in the 1830s; Adolf von Baeyer isolated quercetin from onion skins in 1857, which was an important early contribution to the field.

1. Structural Elucidation (Early 20th Century)

The structures of flavonoids were first defined as a specific class of compounds in the 1920s and 1930s. This outlined structural features common to many of the compounds and classified different types of flavonoids such as flavonols, flavones, and isoflavones.

1. Enzymatic Pathways (Mid 20th Century)

The middle decades of the century found the attention of researchers in the biochemical pathway of flavonoid biosynthesis. In the 1930s to the 1950s, a few key enzymes were identified in the transformation of phenylalanine into flavonoids, namely PAL and CHS, which would later be the foundation of the genetic studies.

1. Molecular Biology and Genetics (Late 20th Century)

Molecular biology methods were identified in the 1980s to clone genes associated with the biosynthesis of flavonoids. Significant discoveries came from the profiling of individual genes involved in specific enzymatic steps, thereby allowing a better understanding of how the production of flavonoids is regulated (Koes et al., 1994).

1. Health Significance and Omics Methods (21st century)

The application of omics technologies, for instance, genomics, transcriptomics, and metabolomics, has further elucidated the complexities of flavonoid biosynthesis, with clarifications about environmental stresses and their impact on the regulation of production in plant organisms. Beyond their health-promoting properties, the antioxidant and anti-inflammatory properties of flavonoids have been explored to date. This would, therefore, mean that the application of flavonoids in food products would be an immense source of health benefits and could even become a means of preventing oxidative stress, which is reported as the leading cause of an organism's degeneration and death.

 6. Current Trends and Future Directions

Continuing recent studies, the possible therapeutic effects of flavonoids on human health and the interest behind sources of flavonoids in diets, as well as their impact on chronic diseases, have been addressed. Integration of systems biology approaches has opened new avenues into flavonoid metabolism and regulation.

1. **BIOSYNTHESIS OVERVIEW**

General Biosynthetic Pathway of Flavonoids

Biosynthesis of flavonoids begins with the molecule phenylalanine and proceeds directly from the next key essential steps in the crucial enzymic reaction:

The reaction between phenylalanine and the enzyme phenylalanine ammonia-lyase transforms it to results in the production of cinnamic acid.

Cinnamic acid is then hydroxylated by the enzyme cinnamate-4-hydroxylase to produce p-coumaric acid.

P-coumaric acid is activated to give p-coumaroyl-CoA, by the enzyme 4-coumarate-CoA ligase (4CL).

The chalcone synthase (CHS) catalyses the condensation of p-coumaroyl-CoA with malonyl-CoA to give chalcone.

Chalcone isomerase CHI converts chalcone to naringenin

Multiple pathways exist from naringenin to yield the different types of flavonoids.

* + - * + Flavanones (for example, naringenin to hesperetin)
				+ Flavonols (for example, naringenin to dihydrokaempferol then to kaempferol)
				+ Isoflavones and anthocyanins with other enzyme-catalyzed rearrangements

Major Precursors for Flavonoid Biosynthesis

Flavonoid biosynthesis essentially requires two major precursors- phenylalanine and malonyl-CoA. General accounts on their roles are presented below:

* Phenylalanine
* Source: Phenylalanine is an aromatic amino acid used as the starting material for flavonoid biosynthesis.
* Conversion: It gets converted to cinnamic acid because of the action of phenylalanine ammonia-lyase (PAL). It is an entry point in the pathway of phenylpropanoids and leads further onward to produce various secondary metabolites, some of which include flavonoids.
* Malonyl-CoA
* Source: This malonyl-CoA is produced through the carboxylation of acetyl-CoA by the action of the enzyme acetyl-CoA carboxylase, and it acts as a precursor for carbon chains in a variety of biosynthetic pathways.

Role in flavonoid biosynthesis: Malonyl-CoA is the co-substrate for the condensation reaction catalysed by CHS in flavonoid biosynthesis. Here, the enzyme CHS catalyses the condensation of malonyl-CoA and p-coumaroyl-CoA to yield the central intermediate chalcone.

1. **KEY STEPS IN FLAVONOID BIOSYNTHESIS**

Phenylpropanoid Pathway

The phenylpropanoid pathway is but one of the very important routes for the biosynthesis of the very large numbers of plant secondary metabolites, among which can be named flavonoids, lignins, and phenolic acids. More detailed step-by-step description of these steps includes the transformation of phenylalanine to cinnamic acid and the production of p-coumaroyl-CoA:

1. Transformation of Phenylalanine to Cinnamic Acid
* Enzyme: Phenylalanine Ammonia-Lyase (PAL)
* Reaction: Catalyses the deamination of phenylalanine to yield cinnamic acid, with ammonia released.
* Importance: This is the regulation point within the pathway. The activity of PAL itself determines the flux toward the end products: phenylpropanoids.
1. p-Coumaroyl-CoA Synthesis
* Cinnamate-4-Hydroxylase (C4H)
* Reaction: Cinnamic acid is hydroxylated at the 4-position to form p-coumaric acid.
* Importance: This is where the first hydroxyl group is introduced, hence making it somewhat more reactive and a precursor to further transformations.
* 4-Coumarate-CoA Ligase (4CL)
* Reaction: p-Coumaric acid activates CoA to give p-coumaroyl-CoA. The reaction is associated with the formation of AMP and pyrophosphate from ATP.
* Significance: p-Coumaroyl-CoA is important in the biosynthesis of flavonoids, lignins, and other phenolic compounds.

These steps are important for activating the phenylpropanoid pathway, leading to a wide array of secondary metabolites of plants, performing vital functions like defense, pigmentation, and structural life processes.

Chalcone Synthase (CHS) Pathway

Condensation reaction

* + - * + Enzyme: Chalcone Synthase (CHS)
				+ Reaction: CHS catalyzes the condensation of one molecule of p-coumaroyl-CoA with three molecules of malonyl-CoA. The product resulting from this condensation is the linear chalcone structure called naringenin chalcone.
				+ This is an important step of flavonoid biosynthesis because chalcones that are produced serve as precursors to other compounds, including flavanones, flavones, and anthocyanins.

Chalcone Biosynthesis

* + - * + The primary flavanone product, naringenin chalcone, is acted upon by the enzyme chalcone isomerase, or CHI, and is further isomerized to produce a major flavanone compound known as naringenin.

Chalcone Isomerization

Chalcone isomerization is one major biochemical process in flavonoid biosynthesis, including chalcone-to-flavanone conversion. In this experiment, the enzyme catalyzing this conversion is the chalcone isomerase, which catalyzes the isomerization of chalcone to naringenin.

**Important Notes on Chalcone Isomerization:**

* Substrate: Chalcones are open-chain flavonoids whose backbone is a phenylpropanoid.
* Product: Naringenin is a type of flavanone, being a subgroup of flavonoids, that bears numerous health benefits and is abundant in many fruits.
* Enzyme: Chalcone isomerase (CHI), catalyzing the stereochemical transformation with the help of intramolecular cyclization of the C-ring

**Mechanism of Action:**

* Binding: The substrate chalcone binds with the active site of CHI
* Cyclization: CHI is involved in the formation of the C-ring; in this regard, this step is a crucial step in the subsequent transformation into naringenin.
* Proton transfer: It aids in the stabilization of the transition state and allows for product rearrangement by making proton transfer feasible during catalysis.
* Product: The product that is generated and released is naringenin.

**Significance**

* Biosynthesis of Flavonoids: This reaction is in the biosynthetic pathway of flavonoids and thus contributes to the amounts of these compounds in plants.
* Health Importance: Naringenin has been associated with several health importance, such as antioxidant activities, medicinal values, and many others.
* While it is an enzymatic process, so fundamentally different from most industrial food manufacturing processes, the process opens up perspectives in plant biochemistry and impacts agricultural practice and nutraceutical development.

Diversification of Flavonoids

Of all these functions, hydroxylation and glycosylation are the most fundamental in flavonoid diversification for their defense roles, pigmentation, and signaling functions. Therefore, it means a number of key enzymes and pathways are implicated.

**Hydroxylation**

 Hydroxylation is a process where one or more hydroxyl (-OH) groups are incorporated into the structures of flavonoids. This may influence solubility, reactivity, and biological activity.

**Important Enzymes Involved**

* Phenylalanine Ammonia-Lyase: This is the first enzyme involved in the pathway of biosynthesis of flavonoids, converting the amino acid L-phenylalanine into cinnamic acid.
* Flavonoid 3-Hydroxylase (F3H): The enzyme hydroxylates flavanones to yield dihydroflavonols
* Flavonoid 3',5'-Hydroxylase (F3'5'H): Hydroxylation at both the 3' and 5' positions creates more complicated structures of flavonoids

**Glycosylation**

* Glycosylation: The attachment of sugar molecules in flavonoids provides greater stability, solubility, and bioavailability
* Major Enzymes:
* Flavonoid Glycosyltransferases (FGTs): Add sugar residues to flavonoid aglycones, glucose, rhamnose, or xylose so the glycosides are formed.
* UDP-glycosyltransferases (UGTs): UDP-sugars act as donors for this glycosyl transfer.
* Flavonoid Classes Pathways
* Flavonols: Hydroxylated on positions 3, 4, and 5 within the flavonoid backbone, quercetin and kaempferol, among others.
* Flavones hydroxylation, then glycosylation, leads to flavones apigenin and luteolin among others.
* Isoflavonoids: These are products of a modified phenylpropanoid pathway and usually show characteristic hydroxylation and glycosylation patterns.
* Anthocyanins: Hydroxylation and glycosylation result in anthocyanin pigments causing red, blue, and purple colorations in plants.
1. **REGULATION OF FLAVONOID BIOSYNTHESIS**

Genetic Regulation of Flavonoid Biosynthesis

**Transcription Factors**

Transcription factors are one of the major controlling factors in the pathway of flavonoid biosynthesis, since they govern the transcription of structural genes.

**Important** **transcription factors are:**

* MYB Transcription Factors: They are central regulators that activate structural gene expression within the flavonoid biosynthetic pathway; on other occasions, MYB TFs collaborate with other TFs to enhance flavonoid biosynthesis.
* bHLH (Basic Helix-Loop-Helix) Proteins: bHLH proteins interact with MYB TFs to form regulatory complexes, which play an important role in coordinately expressing flavonoid biosynthetic genes. This is particularly so for anthocyanins and other flavonoids.

**Environmental Factors Affecting Flavonoid Biosynthesis**

Flavonoid biosynthesis is affected by various environmental factors such as:

* Light: This is yet another significant inducer of flavonoid biosynthetic gene expression. UV radiation and visible light may enhance flavonoids for defensive purposes against photodamage.
* Temperature: Temperature variations may also affect flavonoids in terms of their relative amount. High temperatures can encourage an enhancement in flavonoid biosynthesis, though extreme heat stress can lead to alterations in metabolic flux.
* Stress Conditions: The abiotic as well as biotic stresses such as drought and pathogens, would confer stress-responsive transcription factor expression, which further increases flavonoid concentration in response to resistance by the plant to the stress applied.
1. **FUNCTIONAL ROLES OF FLAVONOIDS**

In Plants

**Attraction of Pollinators and Seed Dispersers**

Flavonoids and other pigments play the role of attracting pollinators and seed dispersers. For instance, bright colors often resulting from the accumulation of flavonoids are often responsible for the hues of flowers, fruits, and leaves, signifying nectar and other rewards to pollinators. Seed dispersers can also be attracted to brightly colored fruits, thus improving plant reproduction and genetic variation.

**UV Protection: Mechanisms of Photoprotection**

UV light causes cell damage in plants. Flavonoids protect the cells through mechanisms

* Absorption of UV Radiation: UV-absorbing flavonoids absorb UV light, protecting DNA and proteins in plant cells from damage.
* Scavenging of Free Radicals: The flavonoids can neutralize ROS that are produced upon UV light irradiation, thus reducing oxidative stress and cellular damage.
* Modulating Growth Responses: After UV irradiation, flavonoid levels may be induced and result in structural and orientational modifications of the leaf which further protect against UV damage.

**Defense Mechanisms: Flavonoids have a significant role in plant defense mechanisms:**

* Antimicrobial Activity: A majority of flavonoids are directly antimicrobial; they inhibit the microbial growth of bacteria and fungi.
* Induction of Defense Responses: Flavonoids may induce SAR, thus usually enhancing the plant's global defense response against pathogens.
* Providing a barrier: these compounds enhance the strengthening of the cell walls and synthesis of protective compounds, thus preventing penetration by the pathogen.

Flavonoids in Human Health

**Antioxidant Activity**

* Mechanisms of Action:
* Scavenging Free Radicals: The flavonoids scavenge ROS, and thus prevent the oxidative stress and cellular damage.
* Chelating Metal Ions: They chelate metal ions; hence, free radical consumption reduces.
* Regulating Antioxidant Enzymes: Flavonoids have increased the activation of antioxidant enzymes that include superoxide dismutase and catalase.
* Health Benefits:
* Associated with a reduced risk of chronic diseases such as cancer, diabetes, and neurodegenerative disorders.
* It may extend life span and general health as well.
* Anti-Inflammatory Activity
* Anti-Inflammatory Activities:
* Flavonoids suppress the action of pro-inflammatory cytokines, for example, TNF-α and IL-6
* NF-κB pathway inhibition: They are held to inhibit NF-κB; it is said to be the master controller of inflammation.
* Health Outcomes:
	+ - * Perhaps diseases like arthritis, cardiovascular disease, and inflammatory bowel disease may be relieved.
			* The inflammation could have led to chronic diseases; some of the cases are diabetes and cancers if taken with flavonoids amongst others.
			* Cardiovascular Health
* Scientific Evidence: Flavonoid Intake and Cardiovascular Health Relationship
* Low Blood Pressure: The availability of nitric oxide with enhanced endothelium function boosts flavonoids that lead to vasodilation and lowers the blood pressure.
	+ - * Lipid Profiles: Low LDL cholesterol and low triglycerides
			* Reduced Heart Disease: Epidemiologic case-control studies reported that high-flavonoid intake is associated with a low incidence of coronary heart disease and stroke.
1. **DIETARY SOURCES OF FLAVONOIDS**

1. Fruits:

Berries- blueberries, strawberries, blackberries, rich in anthocyanin flavonoids

Citrus Fruits- oranges, grapefruits, lemons, flavanones, and flavones

2. Vegetables:

Onions: rich in quercetin with many other flavonoids

Kale and broccoli contain a variety of flavonoids which contribute to their health benefits.

3. Tea:

Green Tea: High in catechins, flavonoids whose antioxidant effect is well-documented.

Black Tea: It has theaflavins and thearubigins produced during fermentation.

4. Red Wine:

Rich in resveratrol and other polyphenols that contribute to its antioxidant effects.

Bioavailability: Factors Affecting Absorption and Metabolism

1. Chemical Structure:

- The bioavailability of flavonoids varies significantly in terms of their chemical structure. In general, it is relatively higher than that of flavonols and flavanones while lower than that of flavones and isoflavones.

2. Food Matrix:

Interactions with other nutrients may affect the absorption of flavonoids. For instance, fats may enhance the absorption of certain flavonoids, but fiber may reduce them.

1. Gut Microbiota:

The gut microbiota of an individual may also impact flavonoid metabolism. Some flavonoids require microbial transformation for them to become bioactive.

4. Cooking and Processing:

 The way food is prepared may determine flavonoid content. Cooking can degrade or increase flavonoids depending on the commodity and the kind of cooking.

5. Genetics:

Individual genetic variation in flavonoid metabolism and efficacy is acknowledged to contribute to the variability in health outcomes.

1. **APPLICATIONS IN BIOTECHNOLOGY AND MEDICINE**

**Agricultural Biotechnology: Enhancing Flavonoid Content in Crops**

* Improvement Techniques:
* Gene Manipulation: Other options may be direct application of CRISPR or transgenic approaches that may be targeted to genes associated with the biosynthesis of flavonoids. Over-expression of an essential gene such as CHS, that is chalcone synthase or F3H, that is flavonoid 3-hydroxylase, may further result in a significant enhancement in the content of flavonoids.
* Breeding Programs: Techniques applied in breeding could be applied to select cultivars with increased flavonoid levels. MAS should be considered as an indispensable tool to be used to identify traits that are associated with the biosynthesis of flavonoids.
* Metabolic Engineering: Alteration of metabolic pathways such that their fluxes could be diverted towards production may even include inhibition of competing pathways, thereby releasing precursors towards flavonoid synthesis.

**Nutraceuticals: Development of Supplements and Functional Foods**

Definition: Nutraceuticals are modified, concentrated foods or food components that may be available in addition to basic nutrition to confer health benefits.

Development:

Flavonoid Supplements: Formulations from green tea, citrus fruits, and berries as sources are made into capsules, powder, etc. It benefits consumers by providing various health functions such as anti-oxidant and anti-inflammatory activities. Functional foods are prepared with added flavonoids or formulated to be naturally high in them. They include, for instance, fruit extracts fortified with flavonoids that can be added to yogurt or ingredients in breakfast cereals that are naturally rich in flavonoids.

Health Effects

Antioxidant and anti-inflammatory effects that may possibly reduce the incidence of chronic diseases due to reduced oxidative stress and inflammation. Foods and supplements rich in flavonoids may improve endothelial function, cause a lowering of blood pressure and exert beneficial effects on cardiovascular disease.

1. **FUTURE DIRECTIONS IN FLAVONOID RESEARCH**

### Emerging research: New discoveries in the biology and chemistry of flavonoids

### Really fantastic the recent research was, because it has discovered fantastic findings about the biology and chemistry of flavonoids.

### 1. Metabolomics: This tool discovers complex interactions and transformations of flavonoids within biological systems; such findings would reveal roles in plant metabolism and potential health benefits.

### 2. Synergistic Effects: The current literature emphasizes synergistic effects of flavonoids with other phytochemicals and nutrients. This is the major reason flavonoids, combined with vitamins or other polyphenols, are more beneficial and have greater health effects.

### 3. Flavonoid-Microbiome Interaction: There appears to be an interest in flavonoids towards the interaction they pose with gut microbiota, which modifies their metabolism and bioavailability. The interaction may be fundamental to the health effects and overall efficacy.

### Future areas for research may therefore include therapeutic applications:

### 1. Chemotherapy: Flavonoids have been evaluated for the inhibition of cancer cell proliferation and interference with pathways associated with apoptosis in cancer cells. More research may show that flavonoids selectively target the stem cells in a cancer or that they act as adjuvants that enhance or amplify the effect of some other drug.

### 2. Neuroprotection Flavonoids are useful in the general area of neuroprotection, especially related to age-related diseases, Alzheimer's and Parkinson's disease. The mechanism of action of flavonoids would unlock valuable new areas of therapy.

### 3. Metabolic disorders Flavonoids are new antidiabetic agents because they may improve metabolic disorders, including obesity and 2h type II diabetes. Meanwhile, the research work concerning lipid metabolism, insulin sensitivity, and inflammation will be conducted in the future.

### 4. Chronic Inflammatory Disorders Further research is required on the flavonoids' activity in chronic inflammatory disorders such as rheumatoid arthritis and inflammatory bowel disease. Specific mechanisms may well help establish focused therapies.

### X. CONCLUSION

Besides being of ecological importance in plants, flavonoid biosynthesis has implicative value in human health. In the plant realm, flavonoids play crucial roles in pathogen resistance, protection against UV light, and actinomycin-like functions in attracting pollinators, thus enhancing reproductive success and survival (Koes et al. 1994). They offer almost the same health benefits to humans such as antioxidant and anti-inflammatory values and have been used more appropriately in the treatment of chronic diseases, which incorporates cancers and heart conditions, according to Manach et al. (2004); Bäuerl et al. (2019).

High-quality food products and nutrition result from improved flavonoids in agricultural biotechnology. In addition, the development of nutraceuticals and functional foods that contain flavonoids has led to a very fundamental role in health promotion and prevention.

Understanding and harnessing the biosynthesis of flavonoids has much greater implications for agriculture, nutrition, and public health.

.

**REFERENCES**

Bäuerl, C., et al. "Flavonoids: A Review of Their Anti-Inflammatory Effects." Molecules 24.14 (2019): 2668. doi:10.3390/molecules24142668.

Crozier, A., Burns, J., & Guild, B. "Flavonoids and Health: A Review." Journal of Nutrition 130.4 (2000): 885-892.

Dixon, R. A., & Paiva, N. L. "Stress-Induced Phenylpropanoid Metabolism." The Plant Cell 7.7 (1995): 1085-1097. doi:10.1105/tpc.7.7.1085

Fritz, C., & Rojas, C. "Biotechnology and the Enhancement of Flavonoid Content in Plants." Plants 8.6 (2019): 187.

Hamberger, B., & Koffas, M. A. G. (2000). "The Phenylpropanoid Pathway: A Focus on the Role of the Phenylalanine Ammonia-Lyase." Biotechnology Advances, 18(4), 421-431. doi: 10.1016/S0734-9750(00)00037-6

Harborne, J. B. (1988). The Flavonoids: Advances in Research Since 1980. London: Chapman and Hall.

Himangi, M., & Shobana, S. (2021). "Flavonoid Intake and Cardiovascular Health: A Review." Nutrition Reviews, 79(5), 539-558. doi: 10.1093/nutrit/nuz084.

Huang, W. Y., et al. (2010). "Bioavailability of Flavonoids: A Review." Journal of Nutrition, 140(2), 334S-339S. doi:10.3945/jn.109.112034.

Jiang, Y., & Baird, W. (2014). "Cinnamate-4-Hydroxylase and 4-Coumarate

Khan, M. I., & Khandaker, L. (2020). Flavonoids: Potential roles in human health and disease. Current Pharmaceutical Design, 26(3), 372-385. DOI:10.2174/1389201025666191009111546

Koes, R., Quattrocchio, F., & Mol, J. N. M. (1994). "The Flavonoid Biosynthetic Pathway in Plants: A Review." The Plant Journal, 6(6), 1047-1062.

Koes, R., Quattrocchio, F., & Mol, J. N. M. (1994). "The Flavonoid Biosynthetic Pathway in Plants: A Review." The Plant Journal, 6(6), 1047-1062.

Koes, R., Quattrocchio, F., & Mol, J. N. M. (1994). "The Flavonoid Biosynthetic Pathway in Plants: A Genetic Approach." Plant Molecular Biology, 24(5), 759-767. doi:10.1007/BF00023664.

Kumar, S., & Prasad, S. K. (2018). "Flavonoids: A Review of Their Role in Plant Defense Mechanisms." Current Science, 114(6), 1221-1232. doi:10.18520/cs/v114/i06/1221-1232.

Ligase from Plant Systems. Plant Physiology and Biochemistry, 78, 12-135. doi:10.1016/j.plaphy.2014.01.023

Manach, C., et al. 2004. "Polyphenols: Human Nutrition and Health." Critical Reviews in Food Science and Nutrition, 44(4), 295-353. doi:10.1080/10408690490414455.

McDaniels, D. A., & Klein, K. 2017. Flavonoids: Structure, Classification, and Biological Activities. In: Flavonoids: Chemistry, Biochemistry and Applications (pp. 1-25). Wiley.

Nakajima, J., & Oikawa, T. 2016. "Flavonoid Biosynthesis: The Role of the Phenylpropanoid Pathway." Plant Physiology, 170(1), 205-216.

Pang, Y., et al. "Transcriptional Regulation of Flavonoid Biosynthesis in Plants." Plant Physiology 184.4 (2020): 2061-2076. doi:10.1104/pp.20.00712

Rice-Evans, C. A., Miller, N. J., & Paganga, G. "Antioxidant Properties of Phenolic Compounds." Trends in Plant Science 2.4 (1997): 152-159. doi:10.1016/S1360-1385(97)01025-0.

Stafford, H. A. "Flavonoid Metabolism: A Biochemical and Ecological Perspective." Plant Physiology 94.2 (1990): 461-466.

Valle, P., & Codoñer, F. M. (2016). "Chalcone Isomerase: A Key Enzyme in Flavonoid Biosynthesis." Plant Physiology and Biochemistry, 107, 1-9. doi:10.1016/j.plaphy.2016.06.006

Vinson, J. A., & Cai, Y. (2012). "Flavonoids in Fruits and Vegetables: A Review of Their Health Benefits." Journal of Agriculture and Food Chemistry, 60(2), 582-590. doi:10.1021/jf203566j.

Vogt, T. (2010). "Phenylpropanoid Biosynthesis." Molecular Plant, 3(1), 2-20. doi:10.1093/mp/ssp106.

Winkel-Shirley, B. Flavonoid biosynthesis: a colorful model for genetics, biochemistry, and cell biology. Plant Physiology 126, 485-493 (2001). DOI: 10.1104/pp.126.2.485