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AN OVERVIEW ON: CHEMICAL PROFILING OF BIO-ACTIVE PLANT PHENOLIC METABOLITES

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ABSTRACT

Phenolic compounds are the largest group of phytochemicals, and several groups have been found in plant origin. Phenolic compounds are all over the place secondary metabolites with strong biological activity and have received to greater extent attentiveness in recent years. Their sources are mainly plants from cultivated and genuine condition, providing beneficial protective and theraputical extracts. The wide range of biological activity of Phenolic compounds such as antioxidant, anti-inflammatory, antimicrobial, anti atherosclerotic, anti diabetic, anti allergic, prebiotic, anti mutagenic, anti-carcinogenic, cardio protective, immune system support means that new sources of Phenolic compounds are constantly being needed. Plant phenolic compounds play an important role in plants to control the growth and have structural signaling functions. They include substances assigned into the five major groups named phenolic acids, flavonoids, tannins, lignans, and stilbene derivatives. In this review, the biosynthesis process of plant phenolic compounds in plants is outlined in brief, which includes the shikimate, pentose phosphate and phenylpropanoid pathways. This chapter begins with classification of phenolic compounds in a manner followed by going through their chemical properties that are important for their biological activities. The chapter includes methods and updated techniques of analysis and extraction of phenolic compounds. This review provides an updated and extensive overview on their chemical profiles and biological activities of plant phenolic compounds.

KEYWORDS: Phenolic compounds; Phenolic acids; Secondary metabolites; Flavonoids; Tannins; Lignans; and Shikimate.

1. INTRODUCTION

Phenolic compounds are a diverse class of bioactive secondary metabolites and are of high and significant importance. They can be described as compounds that contain a phenol moiety. Phenol itself is a benzene ring that is substituted with a hydroxyl group. Thus, its systematic name is hydroxy benzene.[1] Phenolic compounds display a wide range of biological activities. For instance, they are known to exhibit antioxidants, antimicrobial, and anti-inflammatory properties. They are present in various types of fruits such as apple, banana, orange, mango, peach, papaya, strawberry, pomegranate, watermelon, and pineapple. For example, myricetin (a flavonol) is found in apple, gallic acid(a hydroxy benzoic acid) is found in banana, quercetin(a flavonol) and cyaniding (an anthocyanins) are found in pomegranate, p-coumaric acid (a hydroxycinnamic acid) and Naringenin (a flavanone) are found in orange, vanilic acid (a hydroxybenzoic acid) and resveratrol (a stilbene) are found in strawberry, ferulic acid (a hydroxycinnamic acid) and apigenin (a flavone) are found in mango, and luteolin (a flavone) is found in watermelon and pineapple.[2]

Phenolic compounds are produced in the shikimic acid of plants and pentose phosphate through phenylpropanoid metabolization. In the synthesis of phenolic compounds, the first procedure is the commitment of glucose to the pentose phosphate pathway (PPP) and transforming glucose-6-phosphate irreversibly to ribulose-5-phosphate. The first committed procedure in the conversion to ribulose-5-phosphate is put into effect by glucose-6-phosphate dehydrogenase (G6PDH).[3] On the one hand, the conversion to ribulose-5-phosphate produces reducing equivalents of nicotinamide adenine dinucleotide phosphate (NADPH) for cellular anabolic reactions. On the other hand, PPP also produces

erythrose-4-phosphate along with phosphoenol pyruvate from glycolysis, which is then used through the phenylpropanoid pathway to generate phenolic compounds after being channeled to the shikimic acid pathway to produce phenylalanine.[4]

The chemical composition of a plant product is determined by qualitative chemical analysis using various solvents for extraction. Primarily, extraction methods should be selected and optimized along with the corresponding analytical techniques, including the used solvents, the sources, and the properties of the compound itself. More specific analyses are based on the identification of individual phenolic classes, typically by high-performance liquid chromatography (HPLC) or gas chromatography (GC), and their detection by sensitive detectors, such as mass spectrometry (MS).[5]

2. SOURCES OF PLANT PHENOLIC COMPOUNDS

Today, there is a growing demand from the food, pharmaceutical and cosmetic industries for plants with exceptional metabolic properties, including antioxidant properties and Phenolic compounds rich plants. These plants are obtained from two sources: cultivation and the natural state. Polyphenols are isolated and purified from plants (fruits, vegetables and agricultural by-products) and converted into medicines and supplements.[6]

2.1. Wild-Growing Plants

Wild plants are still a readily available but not fully explored source of bioactive compounds with potential phytotherapeutic benefits. The results of selected studies on the phenolic profile of wild-growing plants are presented below *Ageratina petiolaris*. The plant species belonging to family *Asteraceae* is an widespread in Mexico and widely used in traditional medicine for digestive disorders, indigestion, kidney disease, rheumatism and nervous disorders, among others. *Ageratina petiolaris* samples collected in situ have higher Phenolic compounds contents than plants grown ex-situ. Interestingly, the production of gallic acid and rutin was not sufficiently detected in the cultivated samples and was found in the samples from the natural state.[7] It indicates a possible plant response mechanism in modifying biosynthetic processes related to stress conditions in the growing environment. Species of the genus are valued in worldwide folk medicine, e.g., in South Africa, America, India, China and Turkey. The genus *Sideritis*, in the family *Lamiaceae*, includes herbaceous plants growing mainly on the Mediterranean coast, where 140 native species are known. The biological activities of *Sideritis* herb extracts, mainly antioxidant and antimicrobial, are related to the high content of total phenols and chlorogenic acid. According to *Bardakci et al.* assessed the phytochemical composition and antioxidant potential of S. congesta extracts and found the presence of 22 active phenolic metabolites (*Table 1*). The ethyl acetate fraction had the highest phenolic compound content as expressed as gallic acid equivalent (GAE)) for antioxidant activity.[8]

Table 1: Some Examples of Phenolic Compounds Found In Wild Plants.[9]

COMPOUND	PLANT SPECIES
A. Apigenin-7-glucoside, Gallic acid	*Ageratina petiolaris*
B. Flavonoids, phenols, tannins	*Pinus nigra Arn. (Pinaceae)*
C. Catechins, flavonoids, hydroxycinnamic acids, tannins	*Rumex spp. (Polygonaceae)*
D. Chlorogenic acid, leucoseptoside A	*Sideritis spp. (Lamiaceae)*
E. Chlorogenic acid, ferulic acid, 3 c acid	*Valeriana carnosa (Sm.) Dufr. (Caprifoliaceae)*

2.2. Cereals

Cereals are an essential food category for many of the world's populations, with an annual production of more than 2700 tonnes when supply and demand are balanced. Whole-grain products are a vital food category in the human diet and are an invaluable source of carbohydrates, proteins; fibre, phytochemicals, minerals and vitamins are depicted in **Table 2**.

Table 2: Phenolic composition of some cereal crops.[10]

COMPOUND	SPECIES
Anthocyanins, flavonoids (kaempferol, morin, naringenin, quercetin rutin), phenolic acids (caffeic acid, chlorogenic acid, ferulic acid)	Maize (Zea mays L.)
Anthocyanins, phenolic acids, proanthocyanidins,	Rice (Oryza sativa L.)
Anthocyanins, flavonoids, phenolic acids (chlorogenic acid, gallic acid, ferulic acid), proanthocyanidins	Sorghum (Sorghum bicolor (L.) Moench)

2.3. Food sources

Phenolic compounds are widespread in food. Fruits and vegetables, such as apples, cherries, oranges, citrus, grapes, berries, peaches, cereals and tomatoes are particularly rich in poly- phenols. Phenolic compounds have received increasing interest in the human health due

to their benefit effects against several diseases like cancers attributed in particular to their antioxidant activity are depicted in **Table 3**.[11]

Table 3: Food sources of some phenolic compounds.[12]

PHENOLIC COMPOUND	FOOD SOURCES
1. Phenolic acids 2. Gallic acid 3. Ellagic acid 4. Hydroxybenzoates 5. p-Hydroxybenzoic acid 6. protocatechuic acid 7. Vanillic acid 8. Syringic acids	Berries, particularly raspberries, strawberries, and blackberries, grape juice and cereals.
1. Flavonols 2. Quercetin 3. Kaempferol 4. Myricetin Isorhamnetin	Onions *Allium cepa*, apples, plums, cranberries, strawberries, grapes, kale, broccoli, celery stalks, tomatoes, buckwheat, endive, leeks, lettuce, olive, pepper, red wine, green tea and grape juice.
1. Flavones 2. Apigenin 3. Luteolin	Celery, parsley, artichoke, green olive, sweet peppers, onion, garlic, chamomile tea, Thai chili, citrus fruits, celery and spinach.
1. Flavanones 2. Naringenin 3. Hesperetin 4. Eriodictyol 5. Minor compounds 6. Sakuranetin 7. Isosakuranetin	Citrus fruits: orange, lemons, grapes and tomatoes (Naringenin).

3. CHEMICAL PROFILE

Phenolic compounds are a group of small molecules characterized by their structures and carbon skeleton having at least one phenol unit. Based on their chemical structures, phenolic compounds can be divided into different subgroups.[13] The individual class of compounds are describe below.

3.1. Phenolic acids

Phenolic acids are a class of organic compounds that contain a phenol ring (a benzene ring with a hydroxyl group, -OH) and a carboxylic acid group (-COOH). The naming conventions that we've described are commonly used to classify phenolic compounds based on the location of the carboxylic acid functional group relative to the phenol ring.[14]

3.2. Hydroxy benzoic acids

These are phenolic compounds where the carboxylic acid functional group is directly attached to the phenol ring. The term "hydroxybenzoic acid" refers to a group of compounds that are derivatives of benzoic acid and have hydroxyl groups in addition to the carboxyl group, as for example salicylic acid and its derivatives.

Dihydroxybenzoic acids are a subgroup of benzoic acids in which the benzoic acid structure is substituted with two hydroxyl (-OH) groups.[15]

Trihdyroxybenzoic acids are benzoic acids that are substituted with three hydroxyl groups. Examples include 2, 4, 6-trihydroxybenzoic acid and 3, 4, 5-trihydroxybenzoic acid, as for example gallic acid.[16]

4. Hydroxycinnamic Acids

These are phenolic compounds where the carboxylic acid functional group and the phenol ring are separated by a chain of two doubly bonded carbons, which forms a C=C bond with alkene like molecule. Hydroxycinnamic acids are a subgroup of cinnamic acids and include compounds like caffeic acid, ferulic acid, and p-coumaric acid.[17]

5. Hydroxy coumarins

Coumarins are a class of aromatic compounds with a benzene ring fused to an alpha-pyrone ring. Hydroxy coumarins are a type of coumarins that have hydroxyl (-OH) groups substituted onto their structure.[18]

6. Tannins

Tannins are a group of polyphenolic compounds commonly found in various plant tissues, such as fruits, leaves, and bark. They have astringent properties and are known for their ability to bind to proteins and other organic compounds.[19]

6.1. Hydrolysable Tannins

These tannins are large molecules that can be broken down by hydrolysis into smaller phenolic compounds. They consist of a central polyol core (such as glucose) to which multiple gallic acid or ellagic acid units are attached, as for example Gallo tannin & Ellagitannins.[20]

6.2. Condensed Tannins (Pro-anthocyanidins): These tannins are formed by the polymerization of flavonoid units, particularly catechins. They consist of multiple flavonoid units linked together. Condensed tannins are commonly found in foods like tea, red wine, and certain fruits.[21]

6.3. Complex Tannins

These are tannins that have properties of both hydrolyzable and condensed tannins. They have complex structures and are not as extensively studied as the other two types.[21]

7. Lignans

Lignans are indeed composed of two phenolic units that are linked together by a bridge of four carbon atoms. This structure gives them their characteristic arrangement. Examples - Matairesinol, secoisolariciresinol and pinoresinol.[22]

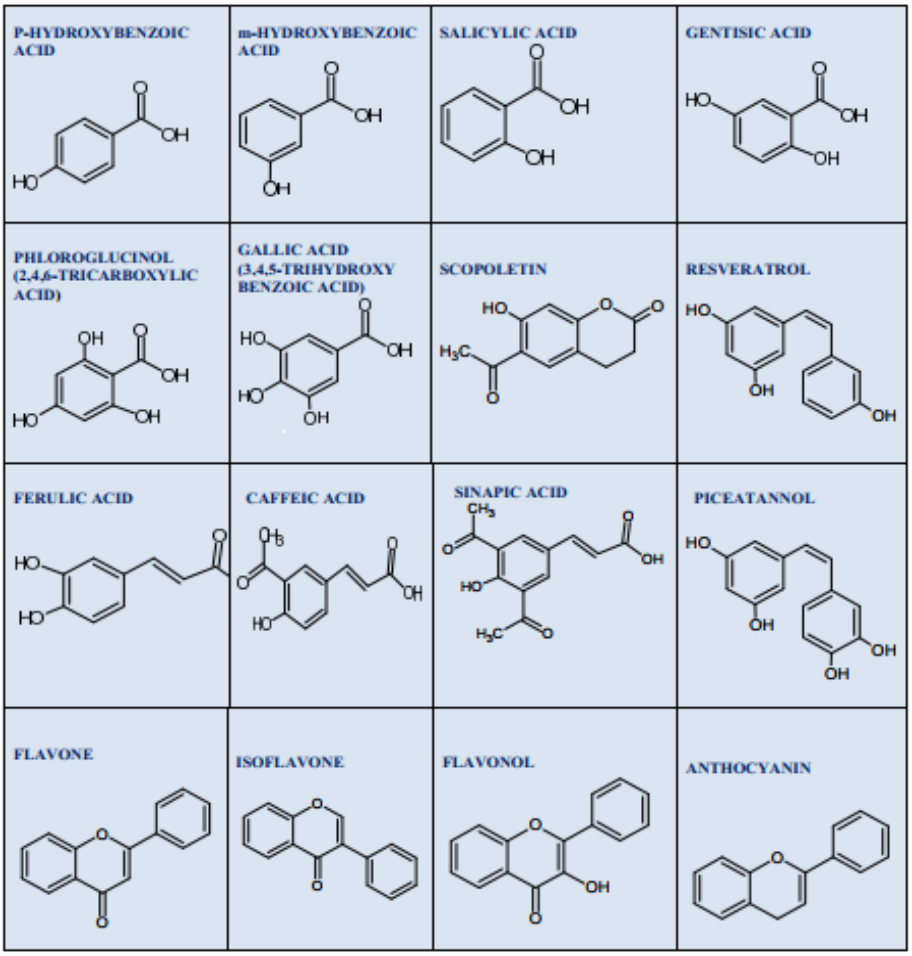
8. Flavanoids

Flavonoids are a series of compounds with diphenylpropanes (C6–C3–C6) as the basic skeleton and 2 aromatic rings connected to each other through the central 3-carbon bridge. The main classes of flavonoids include flavones, flavonols, flavanones, and flavan-3-ols (also known as catechins), anthocyanins, and isoflavones, among others. Each class has variations in the arrangement of functional groups on the flavan backbone, giving rise to the diversity of flavonoid compounds found in plants.[23]

9. Stilbenes

Stilbenes are a class of phenolic compounds, naturally found in a wide variety of dietary sources such as grapes, berries, peanuts, red wine, and some medicinal plants. There are several well-known stilbenes including resveratrol, pterostilbene, and 3′-hydroxypterostilbene.[24] The structure several secondary phenolics are highlighted in **Table 4**.

Table 4: The structure various plant Poly phenolic compound.



4. BIOSYNTHESIS OF PLANT PHENOLIC COMPOUND

Plant materials with an aromatic ring that has one or more hydroxyl groups on it are known as phenolic compounds. Approximately 8000 plant phenolics are found naturally, with flavonoids making up half of this total. Two metabolic mechanisms are involved in the synthesis of phenolic compounds: the shikimic acid pathway, which forms phenylpropanoid, and the acetic acid pathway, which mostly produces simple phenols. The routes involved in the formation of phenolic metabolites are depicted in the following **Figure 1**.

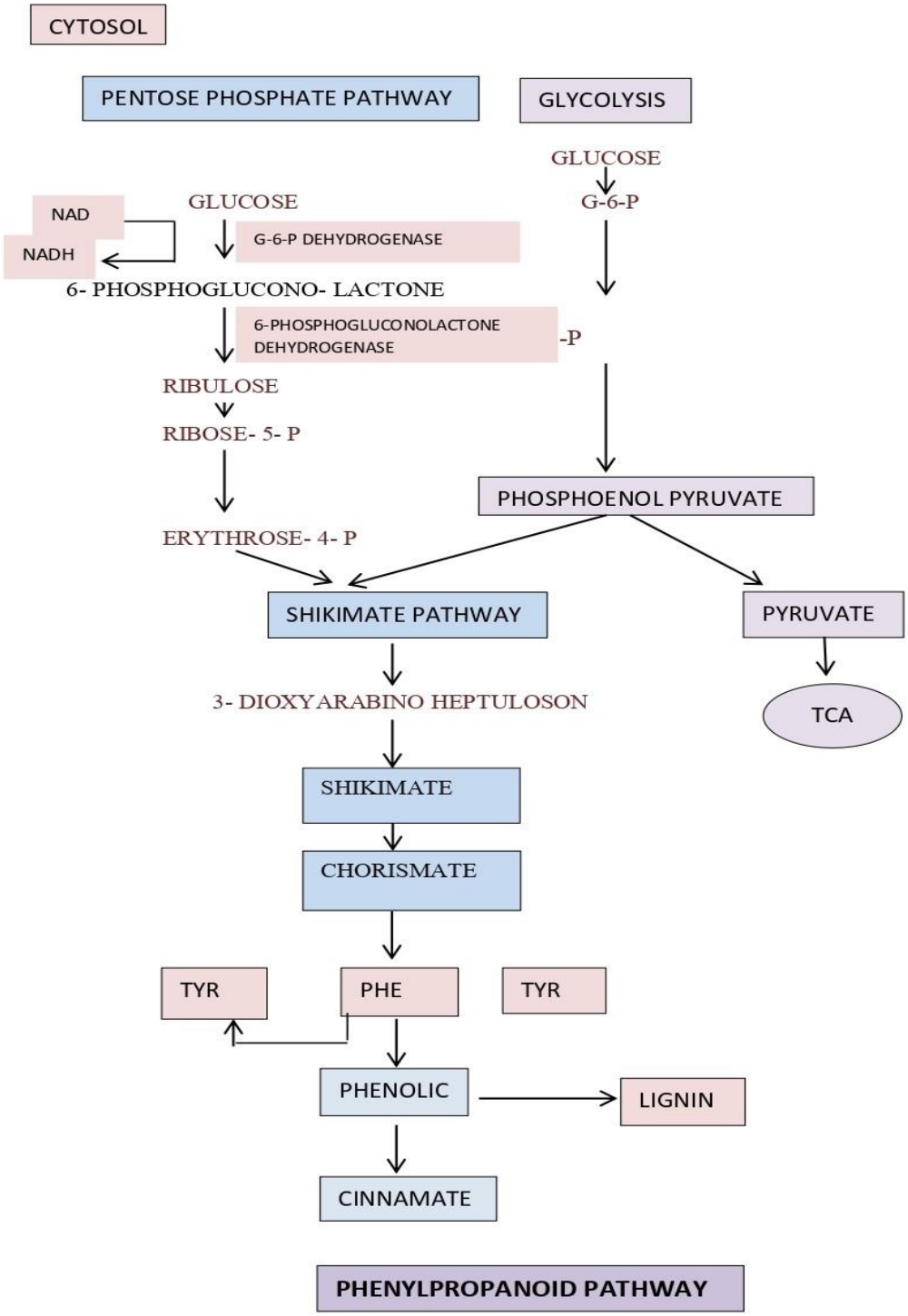


Figure 1: Biosynthesis of phenol compounds in the pentose phosphate, shikimate and phenylpropanoid pathway of plants.[25,26]

5. EXTRACTION METHODS OF PLANT PHENOLIC COMPOUND

The qualitative chemical analysis of plant products involves the use of various solvents for extraction. When it comes to extracting bioactive phenolic compounds from a diverse range of plant materials, including herbs, fruits, and vegetables, researchers employ various techniques and methodologies. These methods encompass solid-liquid extraction (SLE), ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), supercritical fluid extraction (SFE), all of which find application in the extraction of phenolic compounds from plant materials.[27]

5.1. SOLID-LIQUID EXTRACTION

Solid-liquid extraction (SLE) is the most straightforward and widely employed technique for isolating phenolic compounds from a wide array of plants. In essence, SLE entails the direct extraction of either fresh or freeze-dried plant materials using various solvents like methanol, ethanol, acetone, or the aqueous components of solvent blends. Subsequently, an additional step is necessary, often involving column chromatography or solid-phase extraction, to eliminate unwanted substances from the extract.[28]

For example, acetone has demonstrated its effectiveness in extracting polyphenols from lychee flowers when compared to methanol, water, and ethanol. In contrast, a separate study has shown that water is the preferred solvent for extracting polyphenols from walnut green husks. A recent investigation has indicated that both aqueous and organic solvents yield superior extraction results when compared to using exclusively organic solvents. The existing body of literature has consistently shown that there is no universally accepted solvent considered the optimal choice for polyphenols extraction.[29] However, it is generally accepted that solvents with higher polarity tend to outperform others in terms of polyphenols extraction due to their greater solubility for polyphenols.

5.2. ULTRASOUNDASSISTEDEXTRACTION

Ultrasonic-assisted extraction (UAE) stands out as a highly efficient extraction method, surpassing traditional techniques in multiple aspects. Not only does it enhance extraction yields by harnessing the power of cavitations and improving mass transfer, but it also offers several additional benefits, such as minimal instrumental prerequisites, ease of use, shorter processing durations, and reduced demands for solvents and temperature.[30]

A recent study showcased the UAE method achieving a remarkable maximum extraction yield of 13.20 mg/g dry weight (DW) for polyphenols from spruce wood bark. Moreover, the utilization of UAE was found to enhance the extraction yield of anthocyanins from purple sweet potatoes.[31] Additionally, researchers have explored the application of UAE for extracting phenolic compounds from olive trees by optimizing factors like the ethanol/water ratio, amplitude percentage, and ultrasonication time. As per the previous study, UAE is a simple, efficient, and economical method in the extraction of phenolic compounds.

5.3. SUPERCRITICALFLUIDEXTRACTION

Supercritical fluid extraction (SFE) is recognized as an eco-friendly method for extracting phenolic compounds, known for its ability to selectively extract using supercritical solvents. Supercritical fluids like CO2, ethane, butane, pentane, nitrous oxide, ammonia, trifluoro-methane, and water are commonly employed in this process.[32] In a recent study, researchers have harnessed supercritical CO2 extraction for the retrieval of phenolic compounds from *Hibiscuss abdariffa*. Compared with other conventional and original methods, SFE may consume less toxic organic reagents and extraction times, increase safety and selectivity, and avoid sample oxidization in the presence of air. Various methods employed in extraction of phenolic compound are depicted in **Table 5**.

Table 5: Comparison of Different Extraction Methods of Phenolic Compounds.[33,34,35]

EXTRACTION METHOD	ADVANTAGES	DISADVANTAGES	APPLICATION
SLE	I. Simple. II. Well established and widely used. III. Can be easily applied on an industrial scale.	I. High solvent consumption. II. long extraction time.	I. Catechins II. P-coumaric acid
UAE	I. Easy to execute. II. Uses inexpensive equipment. III. Consumes less solvents. IV. Fast extraction.	I. Generation of excess hydroxyl radicals that may cause degradation of active compounds.	II. Gallic acid III. Rutin IV. Proanthocyanidin.
SFE	I. High selectivity. II. Safer and cheaper solvent. III. Easily controlled extraction conditions.	I. Low total yield. II. Not suitable for extraction of polar active compounds.	I. Anthocyanins gallic acid II. Protocatechuic acid

6. ANALYSIS METHODS OF PLANT PHENOLIC COMPOUND

Phenolic compound quantification depends on different parameters, such as the chemical nature of compounds, extraction method used. With the advancement of analytical science, numerous methods have been used for quantifying phenolic compounds from plant materials, such as Spectrophotometry, HPLC, GC, and their combination.[36]

6.1. Spectrophotometry

Spectrophotometry is a rapid and straightforward technique utilized to quantify phenolic compounds in plant materials, relying on distinct principles for assessing the various components found within these compounds. For numerous years, the Folin–Ciocalteu assay has been a widely employed method for identifying phenolic compounds in plants. This assay is grounded in a chemical reduction process employing reagents containing tungsten and molybdenum. The Folin-Ciocalteu method represents a modified version of the Folin–Denis assay, with slight alterations in the composition of the reagent employed.[37] The fundamental approach for this analysis involves the creation of a phenolic compound extract from the material, followed by the addition of Folin-Ciocalteu reagent, sodium carbonate (ranging from 7% to 35% or 0.1 N), and distilled water. Spectroscopy is the common technique used for quantifying different classes of phenolic compounds because of its simplicity and low cost.

6.2. High Pressure Liquid Chromatography

HPLC is the most used technique for the separation and detection of phenolic compounds. It is a versatile and adaptable instrument with various advantages, such as high selectivity, sensitivity, resolution, precision, and sample behavior. This method's principle lies in the separation of compounds from complex mixtures on the basis of their solubility and/or interaction between a less polar stationary phase and a more polar mobile phase. Thus, some factors affect HPLC analysis of phenolic compounds, such as column types, applied detectors, mobile phase, and the properties of the tested compounds.[38] To obtain information about a specific phenolic compound, it is necessary to compare its retention time with the standard. So, this is a major disadvantage when using the HPLC technique. Recent study have been applied GC–FID (flame ionization detector) to detect carvacrol obtained from *Thymus pulegioides* L. In recent years, GC coupled with MS detector has become widespread in measuring complex compounds because of its high selectivity and sensitivity in quantization.[39]

6.3. Hplc- Mass Spectrometry

Phenolic compounds can be analyzed by HPLC combined with tandem MS. HPLC assisted by MS detection is an advanced analytical technique that exhibits high sensitivity and selectivity. This approach can measure structural information about unknown compounds from crude or partially purified samples of natural sources.[40] Recently, numerous studies on phenolic compounds analyses have been focused on the assessment of methods that involve different couplings between HPLC and MS. In recent years, MS is usually used for the analysis of phenolic compounds because of its high sensitivity and selectivity; in addition, it could provide structural information about unknown compounds. Overall, this technique is currently the best analytical approach to studying phenolic compounds of various biological resources and the most effective tool in analyzing their structure. However, its main disadvantage is the high cost of the device.[41]

7. BIOLOGICAL ACTIVITIES

7.1. Phenolic Compound Against Cancer

Natural polyphenols are inherent substances primarily discovered in fruits and vegetables, constituting the most abundant antioxidants in human diets. The scavenging of radicals by these compounds is connected to the presence of hydroxyl groups being substituted on the aromatic rings of phenolic compounds. The ability to scavenge free superoxide radicals is also exhibited by phenolic compounds, which diminishes the likelihood of cancer and safeguards biological systems from the detrimental consequences of oxidative processes on macromolecules like carbohydrates, proteins, lipids, and DNA. It was found that in addition to their primary antioxidant activity, this group of compounds displays a wide variety of biological functions which are mainly related to modulation of carcinogenesis.[42] Moreover, among the extensively recorded biological attributes of polyphenols, cancer prevention stands out as a prominent feature. Polyphenols exert effects on human cancer cell lines that encompass shielding cells and diminishing either the quantity of tumors or their rate of growth. The mechanisms through which polyphenols, present in fruits, vegetables, and spices that constitute essential components of daily nutrition, exert their anti-cancer effects have been under examination. These compounds may be the basis for development of cancer preventive preparations are highlighted in **Table 6**.[43]

Table 6: Anti-mutagenic and anti-carcinogenic properties of polyphenols.[44]

Dietary polyp henols	Protective effects and mechanisms.	Conditions
1. Chlorogenic acid	Inhibiting the formation of DNA single strand breaks.	In super coiled pBR322 DNA.
2. Quercetin **3. Luteolin**	Blocking EGFR tyrosine kinase activity.	In MiaPaCa-2 cancer cells.
4. Myricetin **5. Apigenin** **6. Quercetin** **7. Kaempferol**	Inhibiting human CYP1A1 activities. -Inhibiting the formation of diolepoxide 2 activation.	Studied on 7-ethoxyresorufin O-deethylase

In chemoprevention, suppression of cell proliferation and induction of differentiation and apoptosis are important strategies, with the induction of programmed cell death currently considered as one relevant target in a prevention of cancer. Apoptosis (programmed cell death) is the process by which cells trigger their self destruction in response to a signal. Programmed cell death plays an important role in the maintenance of biological cells and systems. Apoptosis can be triggered through two main pathways: extrinsic and intrinsic. Extrinsic factors could act in the activation of cell surface receptors, such as tumor necrosis factor (TNF) -alpha that leads to the induction of caspase-8. Intrinsic pathways involved internal cell signaling primarily through the mitochondria.[45] Mitochondria also initiate the regulation system of apoptosis through the intrinsic pathway, involving various protein families such as small mitochondrial-derived activator of caspases (SMACs), inhibitor of apoptosis proteins (IAPs), the B-cell lymphoma 2 protein (Bcl2) family, and maintenance of membrane polarity and integrity. Many dietary phenolic compounds, including quercetin, apigenin, chrysin, silymarin, curcumin, ellagic acid and resveratrol, may block carcinogenesis through induction of apoptosis.[46]

7.2. ANTI-INFLAMMATORY EFFECT

Phenolic compounds are a diverse group of secondary metabolites found in plants, and they are known for their potential health benefits, including anti-inflammatory properties. Some well-known subclasses of phenolic compounds include flavonoids, phenolic acids, stilbenes, and lignans, etc. Research suggests that phenolic compounds exhibit anti-inflammatory effects through various mechanisms.[47] Those are Antioxidant Activity, Inhibition of Enzymes, Modulation of Signaling Pathways, Immune System Modulation, Cellular and Tissue Protection, Interplay with Gut Micro biota. It has been demonstrated that besides the essential antioxidant effect, phenolic compounds reduce lipid peroxidation and DNA damage. A variety of phenolic compounds and stilbene derivatives in different parts of germinated peanut suggests that the peanut sprout exerts high anti - inflammatory effects and may be related to the poly-phenolic content and antioxidant properties. Many phenolic compounds act as antioxidants, which help neutralize harmful reactive oxygen species (ROS) in the body. By reducing oxidative stress, they can mitigate inflammation that arises from the damage caused by these free radicals.[48] Some phenolic compounds inhibit enzymes involved in the inflammatory process are described in **Table 7**.

Table 7: Anti-inflammatory effect of phenolic compound.[49]

PHENOLIC COMPOUND	EXPERIMENTAL MODEL	MECHANISM OF ACTION
1. Myricetin	**A.** LPS stimulated H9c2 cells	I. Reduction in cleaved caspase-3 and Bcl-2 levels II. Increase in Bax levels in H9c2 cells.
2. Quercetin	B. **In vitro** Human colonic epithelial cell line Caco-2 cell	III. Inhibition of NLRP3 activation. IV. Reduced ROS production. V. Reduction in IL-1 and IL-18 levels.
	C. In vivo Acetic acid induced ulcer gastric in male Wistar rats.	VI. Reduction of expression of the pro-inflammatory cytokines TNF-α and IL-6 VII. Inhibition of COX-2

7.3. ANTIMICROBIAL EFFECT

Besides the anticancer and anti-inflammatory activity of plant phenolic compounds, antibacterial activities have also been focused on. Many studies have been conducted on antibacterial activity. The antimicrobial properties of phenolic compounds are due to the ability of their hydroxyl groups to bind the active sites of key enzymes and modify the metabolism of microorganisms.

Antimicrobial activity depends on the position of the hydroxyl substitution in the aromatic ring, as well as on the length of the saturated side-chain.[50] For example, it has been demonstrated that caffeic acid possesses higher antimicrobial activity than p-coumaric acid because the first one has more hydroxyl groups substituted in the phenolic ring. *Bacterial Strains* both cocci Gram-positive and Gram-negative rods bacterial species were selected as test microorganisms according to their pathologic origin like *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Micrococcus luteus*, and *Salmonella typhimurium* were used. Antimicrobial activity of commercial phenolics compounds like Gallic Acid, Quercetin, Caffeic acid, Coumarin, Tannic acid and Catechol was investigated against microorganism and highlighted in **Table 8**.[51]

Table 8: Antibacterial activity of phenolics compound.[52]

PHENOLIC COMPOUNDS	Escherichia coli	Pseudomonas aeruginosa	Bacillus subtilis
Gallic acid	++	++	-
Quercetin	++	++	+
Caffeic acid	++	++	++
Coumaric acid	++	++	+
Tannic acid	++	++	+
Catechol	++	++	+
Chloramphenicol	+++	+++	+++

‘’+’’ = Moderate antimicrobial activity, ‘’++’’ = Clear antimicrobial activity,‘’+++’’ = Strong

7.4. ANTIOXIDANT ACTIVITY

The antioxidant properties of phenolic compounds have displayed great potential, and this potential is closely linked to both the extraction solvent employed and factors such as plant origin, growth conditions, timing of harvest, and storage environment. Investigating the antioxidant capacity of phenolic extracts obtained from various plant species stands as a prominent subject within the scientific community. There are three important systems where phenolic compounds can express their antioxidant activity: in plants, in foods and in humans.[53] Antioxidant action of phenolic compounds is due to their high tendency to chelate metals. Phenolics possess hydroxyl and carboxyl groups, able to bind particularly iron and copper. These properties are reflecting the reducing properties of phenolic compounds and their ability to interact with metal ions and proteins.[54] Specifically, the antioxidant activity of phenolic compounds is manifested through the direct scavenging of reactive oxygen species (ROS), the inhibition of enzymes participating in oxidative stress, the restoration of other antioxidants (such as α-tocopherol), the binding of metal ions accountable for ROS generation, and ultimately, the triggering of intrinsic antioxidant defense mechanisms.[55]

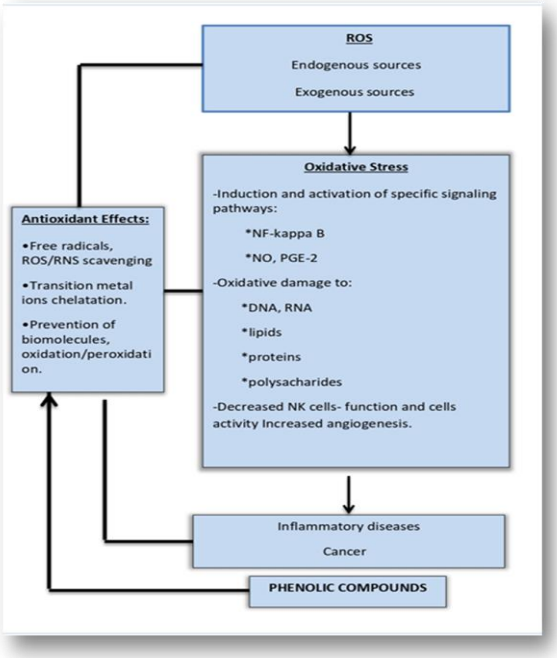


Figure 2: Simplified scheme presenting oxidative stress consequences and the beneficial effects of phenolic compounds.[56]

8. CONCLUSIONS

This review provides in-depth insights into various aspects of phenolic compounds derived from plants, including their categorization, extraction techniques, analysis methods, and biological effects. Phenolic compounds are primarily grouped into phenolic acids, flavonoids, tannins, phenolic lignans, and phenolic stilbenes. In the realm of advanced extraction, techniques such as SLE, SFE, UAE, and MAE are discussed. In contrast, traditional extraction methods, while straightforward and widely employed, are overshadowed by unconventional technologies that offer improved extraction efficiency concerning cost, yield, time, and/or selectivity. Among the array of analytical methods, HPLC takes center stage, particularly when paired with highly sensitive and sophisticated detectors like MS. The proliferation of these detectors heightens both sensitivity and specificity in analyzing the target compounds. This review serves as an invaluable resource for delving into the identification, chemical characteristics, and further exploration of the biological activities associated with phenolic compounds sourced from natural plant products.

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