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Minirvew about phenolic compound and its efficacy for health.

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Abstract

Polyphenolic compounds (PC) are among the most abundant secondary metabolites in nature. They are widely distributed in the world and can be found in fruits, cereals, tea, coffee, and beverages. Polyphenols can act as antioxidants, mainly due to the electron-donating phenolic groups in their structures. The antioxidant function of polyphenols in the prevention of oxidative stress-related cellular and extracellular damage, Polyphenols provide a variety of functions, including antioxidant, antimicrobial, anti-inflammatory, anti-angiogenic, and anti-tumor. The current work aims to needed to fully understand the mechanisms and benefits of polyphenols in various health conditions. Polyphenolic compounds abridge a wide diversity of compounds that are vastly distributed in fruits cereals and beverages. They play important roles in human health, mainly the consumption of food rich in PC is related with many human health benefits, mostly due to the antioxidant activity

Key words : phenolic compound, antioxidant, antiinflammation and human health.

Introduction:

essential for the successful growth and development of most plants, flavonoids and related phenolic compounds can occur in high concentrations in some species and are referred to as secondary metabolites. They are structurally diverse with in excess of 8000 structures having been reported (1), and many are found in only a limited number of species. In planta, they have various functions, including protecting plants from herbivores and microbial infection, as attractants for pollinators and seed dispersing animals, as allelopathic agents, UV protectants, and signal molecules in the formation of nitrogen-fixing root nodules (1,2).The role of flavonoids and related compounds, as components responsible, in part, for the protective effects of a fruit and vegetable-rich diet has become an increasingly important area of human nutrition research(3,4).Unlike the traditional vitamins, they are not essential for short-term well-being, but there is increasing evidence that modest long-term intakes can have favorable effects on the incidence of cancers and chronic diseases, including cardiovascular disease (CVD), type II diabetes, and impaired cognitive function, which are occurring with increasing frequency in human .

Phenolic compounds (PC) are one of the classes of bioactive molecules most studied by the scientific community; these molecules have well-reported health benefits; a daily diet enriched in these compounds is important to promote wellbeing. PC are considered antioxidants due to the donation of a hydrogen atom and/or an electron to free radicals, causing the break of chain reaction of oxidation (5,6). The antioxidant effect depends on the number and position of the hydroxyl groups (7). In organisms, an oxidative process can be responsible for the In generation of free radicals that attack the cells, leading to serious diseases, such as cancer, cardiovascular diseases atherosclerosis, neurological disorders, hypertension, and diabetes mellitus, due to oxidative and nitrosative stress , While the mechanisms remain multifactorial, they include properties affecting nucleic acid, lipid and protein damage, such as non-enzymatic glycation or gloxidative stress, and even may have antiaging properties (8). Polyphenols are effective for a number of diseases such as those stemming from inflammation, oxidative stress (9), pyretic activity (10), reproductive disorders, nervous system disorders, elevated blood glucose (11), microbial and viral infections, cholesterol irregularities, cellular proliferation and tumorigenesis, hypertension, pain management and digestive complications (12) .This review will summarize the different groups of compound that are involved, their fate in the body after ingestion as the pass through the gastrointestinal tract (GIT) and are absorbed into the circulatory system, the evidence of their protective impact on human health .

Polyphenol classification.

Polyphenols are divided into several classes according to the number of phenol rings that they contain and the structural elements that bind these rings to one another. They are classified into two main groups: flavonoids and non-flavonoids. The flavonoids can be divided into six subclasses (flavonols, flavones, isoflavones, flavanones, anthocyanidins, and flavanols (13).The non-flavonoids' main subclasses are phenolic acids, lignans, and stilbenes.

1-The flavonoids compounds:

The term flavonoid derives from the Latin “flavus,” which means “yellow”. Besides their physiological roles in plants, flavonoids have a relevant role in the human diet, where they are the most plentiful class of polyphenols, with more than 9000 different structures identified. Flavonoids are low-molecular weight compounds widely distributed in plants, especially in fruits and vegetables, although they are not considered nutrients. Accordingly, flavonoids can be found in foods and beverages such as artichokes, berries, cherries, citrus fruits, grapes, parsley, soybeans, tea, and wine, yet the richest sources are onions (up to 1.2 g/kg fresh weight) (14,15). The carbon atoms of flavonoids are arranged in a C6–C3–C6 configuration with two aromatic rings (A and B) covalently bound to three carbon atoms, thus leading to the formation of an oxygenated heterocycle ring C (Figure 1). The vast diversity of flavonoid structures arises from the various combinations of multiple hydroxyl groups, methyl groups, glycosides, and acylated group substituents on the basic C6–C3–C6 backbone (14).

Flavonoids can occur in nature as glycosides, as aglycones, or as acetylated, methylated, prenylated, and sulphated derivatives. They can be ascribed to each of the six subclasses, anthocyanins, flavanols (flavan-3-ols), flavanones, flavones, flavonols, isoflavones, and according to the degree of oxidation of the central ring (ring C) and the number and position of hydroxyl groups (16). Flavonoids exhibit antioxidant properties and can protect cells against oxidative damage with biological activity, depending on structural differences and glycosylation (17,18).

Isoflavones bear structural similarities to oestrogens, in particular to 17-β-oestradiol. Isoflavones depict ring B attached to ring C at the C3 position of the latter ring and exhibit hydroxyl groups in the C7 and C4’ positions, akin to oestradiol. As isoflavones can bind to oestrogen receptors, they are classed as phytoestrogens. They are mostly found legumes, e.g., chickpeas, fava beans, or soybeans. The latter is acknowledged as the most plentiful source of isoflavones, where daidzein, genistein, and glycitein, the three most important molecules of this subclass, are included. These occur mostly as glycosides through conjugation with glucose, given the heat sensibility of isoflavones. This often leads to the hydrolysis of the aglycone form during processing and storage. Given that beans are rooted in the diets of numerous cultures, isoflavones have a significant impact on human health (19.20).

The subclasses of flavones, flavonols, and flavanones are the most common and vastly widespread in the plant kingdom (Figure 1). Flavones and particularly their 3-hydroxy derivatives flavonols, including their glycosides and derivatives modified on all three rings, make these the largest subclasses among all polyphenols. Myricetin, kaempferol, and quercetin are among the most widespread flavonols, which are present in the skins of grapes, apples, and blueberries, among other fruits and vegetables. Over 250 glycosidic combinations have been identified for each of the two latter flavonols aglycones (21,22).

Flavanols or flavan-3-ols, often referred to as catechins, differ from most flavonoids since they lack a double bond between C2 and C3, and a C4 carbonyl in Ring C. Combined with these features, the hydroxylation at C3 generates two chiral centres (on C2 and C3), hence four possible diastereomers (23,24).

Flavanones have a 2,3-dihydroflavone skeleton, although they lack a double bond between C2 and C3, thus conveying chirality to the former position. As an outcome, the B ring is not planar, unlike typically conjugated flavones, a feature that is supposed to influence the biological activity of flavanones. They are usually glycosylated by either a disaccharide or a glucoside at C7 to yield flavanone glycoside, and they can be found in high titres in citrus fruits, tomatoes, and some aromatic plants (e.g., mint). They contribute significantly to the daily intake of flavonoids, exceeding that of other polyphenols, and their bioavailability also surpasses that of either flavonols or flavan-3-ols (12,22).

Anthocyanidins and anthocyanins are two of the subclasses of flavonoids, where the former corresponds to the aglycone form and the latter corresponds to the glycoside form. Anthocyanidins, colored, medium-sized molecules, are classed into 3-deoxyanthocyanidins, 3-hydroxyanthocyanidins, and O-methylated anthocyanidins, depending on the presence of hydroxy or methoxy groups bound to the ringed scaffold. Anthocyanins are often found as anthocyanidin glycosides, mostly through condensation with monosaccharides, although di- or tri saccharides may also be bound; additionally, acylated anthocyanins can also be found as an outcome of acylation with organic acids. Anthocyanins are available in several fruits and vegetables and are used as natural colorants in processed foods (red, blue, and purple pigments with low toxicity). Still, their color is strongly influenced by structure and environmental factors, e.g., temperature, light, and ph. Most notably, anthocyanins are red in an acidic environment, yet they shift to blue or purple in an alkaline medium (13,25). Anthocyanins have been shown to display antidiabetic, anti-inflammatory, and antimicrobial activities and to contribute to the prevention of cardiovascular and neurodegenerative diseases (26). The health and therapeutic effects of anthocyanins are by far associated with their antioxidative activities, to which the glycosylated B-ring structure of anthocyanin strongly contributes. Anthocyanidins have higher antioxidant activity than anthocyanins, as the C-ring of the latter bears an extra sugar at C-3, opposite to the former´s single sugar (27). However, while glycosylation decreases antioxidant activity, acylation of anthocyanins with phenolic acid has the opposite effect (28).

2-The non-flavonoid compounds

Non -flavonoid can be divided into two different classes of phenolic acids based on C1–C6 and C3–C6 backbones, which correspond to benzoic and cinnamic acid hydroxy derivatives, respectively, and they are often found in bound form such as amides, esters, and glycosides (22). They have antioxidant activity as chelators and free radical scavengers, with special impact on peroxyl, hydroxyl radicals, and peroxynitrites. Hydroxybenzoic acids are mostly found bound with cell wall fractions, e.g., lignins, and to a minor extent in soluble form (conjugated with sugars or organic acids). Well-known hydroxybenzoic acids include gallic, syringic, p-hydroxybenzoic, and vanillic acids. Their titre in plants is generally low, safe for some berries and vegetables (e.g., horseradish, onions) (13). Hydroxycinnamic acids, examples of which are caffeic acid, chlorogenic acid, coumaric acid, ferulic acid, and isoferulic acid, are found in all parts of plants; their concentration is highest in ripe fruits and vegetables. One of the most abundant hydroxycinnamic acids, chlorogenic acid, which occurs in high concentrations in coffee, is formed by the combination of caffeic and quinic acids. The bound phenolic acids can be hydrolyzed by enzymes or endure acid or alkaline hydrolysis. In addition to their antioxidant role, chlorogenic acid and caffeic acid are also likely to inhibit the formation of mutagenic and carcinogenic N-nitroso compounds, therefore they are supposed to have an inhibitory effect on the N-nitrosation reaction in vitro (10,26).

Stilbenes are a small class of plant secondary metabolites derived from the phenylpropanoid pathway, some of which are associated with mechanisms of defense in the plant. They are found in several edible plants, e.g., some berries, grapes, and peanuts, and have a distinct structure consisting of two aromatic rings linked by an ethylene molecule. The main representative of stilbenes is resveratrol (cis and trans), which is found in high concentrations in the fresh skin of red grapes. This particular stilbene has been thoroughly studied in the last two decades, which highlighted that its intake brings health benefits due to its cardiovascular, chemopreventive, antiobesity, antidiabetic, and neuroprotective properties (23). Notwithstanding, other stilbene compounds, e.g., pterostilbene, a resveratrol analogue, have been suggested to display improved neuroprotective effects as compared to resveratrol (11).

Lignans are plant secondary metabolites synthesized by oxidative coupling of two phenylpropane units and occur mostly in the free form, with the glycosylated form occurring sparingly; oleaginous plants, and particularly their seeds (e.g., flaxseed, sesame, linseed, and sunflower) are rich in lignans, but fibrous plants, e.g., rye, whole wheat, vegetables, and fruits are also dietary sources of lignan, albeit at minor amounts (20). It has been shown that the gut microbiota is able to transform dietary lignans through deglycosylation and demethylation into human lignan agents such as enterodiol and enterolactone. These may act as therapeutic agents in cancer chemotherapy and neurodegenerative diseases, features that in recent years have raised major interest in lignans and synthetic derivates (7,26) .

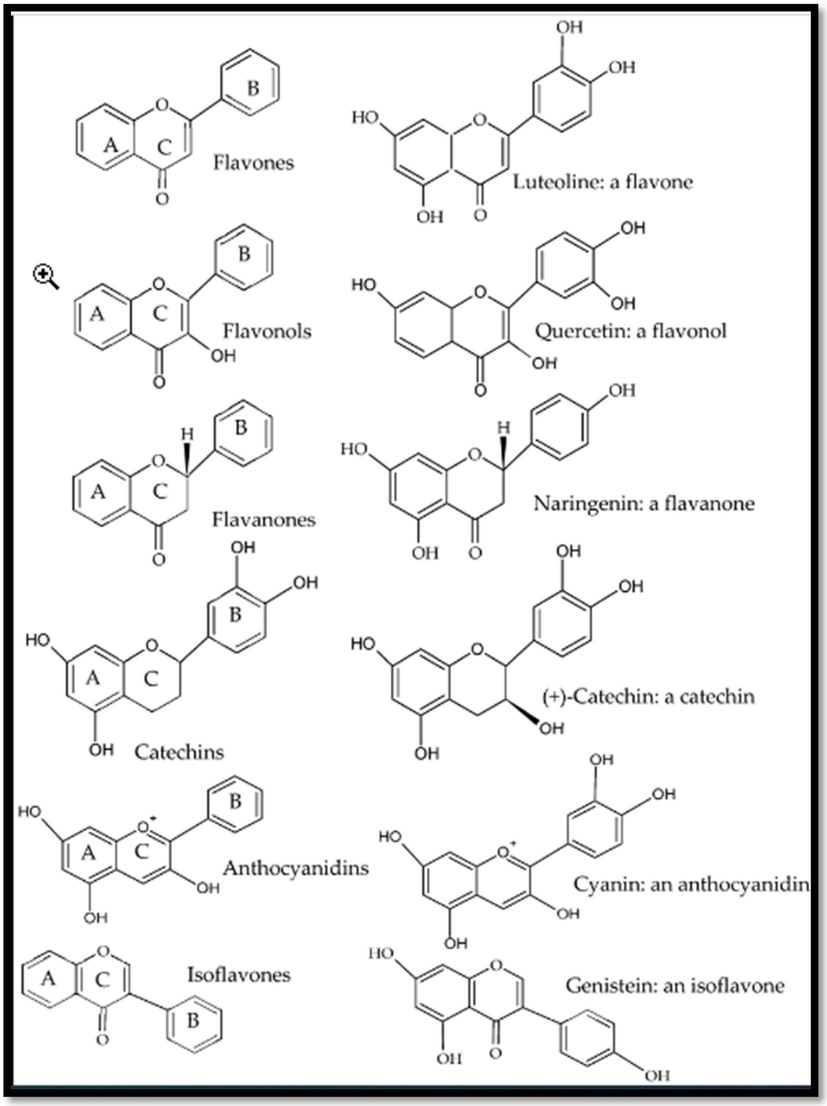

Figure 1. Subclasses of flavonoids: basic structure and a representative example.

Potential health effects of polyphenols:

Polyphenols may protect cell constituents against oxidative damage and, therefore, limit the risk of various degenerative diseases associated with oxidative stress. In fact, they have important roles in plant defense mechanisms against viruses, bacteria, fungi, and herbivores (29) the health benefits of dietary polyphenols have attracted much attention, mainly due to their accessibility in our daily food intake (30) Moreover, polyphenols in foods may affect the organoleptic properties, as they can contribute to the bitterness, astringency, color, flavor, odor, and oxidative stability of foodstuff, particularly flavonoids, have been associated with improved cardiovascular health. They can help reduce oxidative stress, inflammation, and the risk of developing cardiovascular diseases such as heart disease and stroke (29).

1- **Epigallocatechin gallate** (EGCG): EGCG is a catechin and a major polyphenol found in green tea. It exhibits potent antioxidant and anti-inflammatory properties and has been associated with numerous health benefits. EGCG has shown potential in reducing the risk of cardiovascular disease, obesity, diabetes, and certain types of cancer (7,8).

2- **Quercetin**: Quercetin is a flavonoid found in various fruits, vegetables, and grains. It possesses antioxidant, anti-inflammatory, and anticancer properties. Quercetin has been linked to cardiovascular protection, immune modulation, and potential benefits in managing conditions like allergies, asthma, and neurodegenerative diseases (9).

3-Curcumin: Curcumin is a polyphenol found in turmeric, commonly used as a spice in Indian cuisine. It possesses potent antioxidant, anti-inflammatory, and anticancer properties. Curcumin has shown potential in the prevention and management of chronic diseases, including cancer, neurodegenerative disorders, and cardiovascular diseases (10).

4-Resveratrol: Resveratrol is a polyphenol found in grapes, berries, and red wine. It exhibits antioxidant, anti-inflammatory, and anticancer properties. Resveratrol has shown promising effects in various preclinical studies, including cardiovascular protection, neuroprotection, and potential anti-aging effects (11).

5-Anthocyanins: Anthocyanins are a type of flavonoid responsible for the vibrant colors in many fruits and vegetables, such as berries, cherries, and purple sweet potatoes. They possess potent antioxidant and anti-inflammatory properties. Anthocyanins have been associated with various health benefits, including cardiovascular protection, anti-obesity effects, and cognitive enhancement (12).

Mechanical health effects of polyphenols:

1- Biological Activities of Polyphenols and Health Benefits:

Oxidative stress is considered to play a pivotal role in the pathogenesis of aging and several degenerative diseases, such as atherosclerosis, cardiovascular disease, type II diabetes, and cancer. Several studies describe polyphenols as having many activities and properties, including antioxidant, anticarcinogenic, anti-inflammatory, modulators of immune system response, and protectors of the cells against free radical damage (30). Body cells and tissues are continuously threatened by the damage caused by free radicals and reactive oxygen species (ROS), which are produced during normal oxygen metabolism or are induced by exogenous damage. Flavonoids can act because of another mechanism, through the interaction with various enzyme systems.

They have been reported to possess many useful properties, including anti-inflammatory activity, estrogenic activity, enzyme inhibition, and antimicrobial activity(31). Irrespective of their specific nature and intended role, for the biological activity of PC to be advantageously used, their structure must be preserved, and they have to be available for systemic circulation (bioavailability). The preservation of the structure strongly depends on the PC extraction and enrichment methods (e.g., classic liquid extraction, supercritical extraction, pressurized liquid extraction, membrane technology for purification) as described elsewhere (30), but the outcome of those treatments also impacts bioavailability, since the latter depends on the interaction with the food matrix, besides the metabolic processes mediated by the liver, intestine, and microbiota(32). Additionally, PC metabolites produced either in vivo or in vitro may have improved biological activity(33,34). Adequate formulations, namely through PC encapsulation (30,35)or PC conjugation(34), e.g., with gellan gum(33), and the advantageous use of synergistic effects(32,31), have been shown to increase the biological activity of PC. Despite the well-acknowledged benefits of PC in health, as neatly summarized in a recent review(21) ,some side effects and toxicity associated with PC consumption have also been reported [36]. These are typically associated with intakes in dosages largely exceeding what is recommended, namely in Western diets (36,30) and have been summarized as carcinogenicity/genotoxicity, the estrogenic effect of isoflavones, thyroid toxicity, interactions with pharmaceuticals, and negative nutritional effects, the latter namely through the lack of proper synergistic effects with other dietary items (7). Specific details can be found elsewhere (37). Still, it is highlighted that inconsistency of results in human studies are often observed, which can be ascribed to the inter-individual variability in bioavailability and bioactivity of dietary polyphenols, alongside with the heterogeneity of the populations study and the statistical approach of the studies (30,36).

2- Antioxidant Activity

Among the notable bioactivities of PC, the antioxidant activities have been widely studied, including the scavenging of free radicals, inhibition of lipid oxidation, and reduction of hydroperoxide formation, among others. Details on the different methods to assess antioxidant activity in vitro are discussed elsewhere in a comprehensive review (38). Transition metals can function in various oxidation processes, acting as a catalyst in the autoxidation of many biomolecules. In many cases, oxidation can be initiated by the hydroxyl radical (OH·) generated in the reaction between iron and hydrogen peroxide, known as the Fenton reaction. Metals can also generate other ROS. PC have the ability of chelating metals and controlling their prooxidant activity. Polyphenols are known to be agents that can scavenge a wide range of ROS by mechanisms that include direct scavenging of ROS, suppression of ROS formation by inhibition of enzymes involved in their production, inducing endogenous antioxidants enzymes, regeneration of body antioxidants such as α-tocopherol and ascorbic acid, regulation of signal transduction and up-regulation or protection of cellular antioxidant defense systems. As antioxidants and anti-inflammatory agents, PC act at a local level when they act directly during passage through the gastrointestinal tract, as well as at a systemic level after their absorption (11,38). Further details on the mechanistic action of PC as antioxidants can be found elsewhere (36).

Almost every group of flavonoids (Figure1) can act as antioxidants. Free radicals can damage cells by lipid peroxidation, resulting in cellular membrane damage leading to swelling and eventually death. Protection mechanisms of the body include enzymes such as superoxide dismutase, catalase, and glutathione peroxidase and other non-enzymatic materials such as glutathione, ascorbic acid, and α-tocopherol. Flavonoids have an additive effect on endogenous scavenging compounds. Flavonoids are oxidized by radicals, resulting in more stable, less reactive radicals. In other words, flavonoids stabilize the ROS by reacting with the reactive compound of the radical. Some of the flavonoids can directly scavenge superoxide, whereas other flavonoids can scavenge the highly reactive oxygen-derived radical called peroxynitrite, also can chelate iron removing a causal factor for development of free radicals. Another interesting effect of flavonoids on enzyme systems is the inhibition of the metabolism of arachidonic acid (39,40). This feature gives flavonoids anti-inflammatory and antithrombogenic properties. Selected flavonoids, namely quercetin, kaempferol, and myricetin, effectively inhibited platelet aggregation in dogs and monkeys. Several studies have been published to correlate the intake of PC through food ingestion and antioxidant activity both in vitro and in vivo, although the former largely exceeds the latter (35.40). As an example, Zujko and Witkowska evaluated the total PC titre in different beverages (e.g., red and white wine, different teas, orange juice, beer), several types of chocolate, and several nuts and seeds (e.g., walnuts, sunflower seeds, pistachios) and determined the corresponding antioxidant potential with the ferric reducing antioxidant power (FRAP) method. It was possible to establish that in all cases the increasing PC titer resulted in increased antioxidant potential. The highest values in each class tested were observed for red wine, dark chocolate, and walnuts(18). In another study, Lafarga and co-workers also addressed the relationship between total PC titer and antioxidant potential, using the FRAP and 2,2-diphenyl-1-picrylhydrazyl (DPPH) methods of dry and cooked pulses, e.g., lentils, faba beans, chickpeas, and soy(20). Again, the total PC titre correlated positively with antioxidant potential with the best result being observed for faba beans. Moreover, the authors established that cooking increased total PC titre and antioxidant activity in methanolic extracts, which was attributed to cell disruption and improved extraction of polyphenols. Finally, simulated gastrointestinal digestion led to a further increase in total PC titre and antioxidant potential of the extracts evaluated, which was attributed to enhanced bio accessibility to PC. Recently, an in vivo study demonstrated that winemaking by-products from Syrah grapes, rich in anthocyanins, flavanols, flavonols, and stilbenes (Figure1), displayed higher antioxidant activity than red wine, leading to lower very low-density lipoprotein cholesterol titres (33) Previously, an ex vivo had demonstrated that LDL-cholesterol oxidation (ex vivo) was lower in healthy human subjects due to daily intake of daily intake of 3 g guarana seed powder containing 160 mg catechins(37). A more recent ex vivo study showed that a nutraceutical formulation based on a polyphenolic-rich extract from winemaking by-products (Taurisolo®) displayed high oxidant power, given its action as a ROS scavenger agent. This action ultimately triggered an increase of antioxidant enzyme activities in the intracellular medium, which was tentatively related to the up-regulation of their gene expression (39). Despite the acknowledged antioxidant role of PC, their dietary intake at high doses, e.g., through dietary supplementation, may have a deleterious effect, such as pro-oxidant activity, production of ROS and hydrogen peroxide, and oxidative stress (40).

3.Neurodegenerative Protective Effects

Many neurodegenerative diseases, including Alzheimer’s disease, consist of damage to cellular components such as DNA, lipids, and proteins. In these conditions, oxidative stress is considered as a key regulatory factor. The oral administration of green tea polyphenols and flavonoid-related compounds has been shown to inhibit iron-induced lipid peroxide accumulation and age-related accumulation of neurotoxic lipid peroxides. Accordingly, the risk of the development of Parkinson’s disease is reduced by the consumption of polyphenols in the form of green tea(41). Epidemiological studies suggest that polyphenols may be effective in reversing neurodegenerative pathology and age-related declines in neurocognitive performance (35,38) Flavonoids (Figure 1) may perform a key role in the enzyme and receptor systems of the brain, exerting significant effects on the central nervous system. Flavonoids can inhibit enzymes such as aldose reductase and phosphodiesterase and prevent neurodegenerative diseases.

Preparations containing flavonoids as the main physiologically active agent have been used for centuries by physicians and lay healers as tools to tackle human disease. The release of arachidonic acid is a starting point for a general inflammatory response. Flavonoids inhibit the metabolism of arachidonic acid through the enzyme pathway, thus conveying flavonoids’ anti-inflammatory and anti-thrombogenic properties (22,26). The positive effects of PC (both observed and potential) in neurodegenerative diseases, including the use of PC-rich foods, have been described in a recent comprehensive review (42). In this work, the authors highlight that the neuroprotective effect of PC can be either direct, through the action of PC that crosses the blood-brain barrier, or indirect, through PC that influence the gut microbiota. The latter rely on the two-way communication between the gut and the brain through the neural, endocrine, and immune systems, the so-called brain-gut axis, to ultimately play a neuroprotective role (22,5). Some authors, however, suggest that care must be taken when relating the intake of PC-rich foods, e.g., walnuts with protective neurodegenerative effects (42). Positive effects were only observed for some populations, and further studies were suggested to fully understand the mechanisms of neuroinflammation inhibition in neurodegenerative diseases. Moreover, a large number of clinical trials are needed to validate the translation of the observed effect to humans. A systematic review performed by Colizzi, using as ref. (24) studies, failed to find enough evidence that polyphenols have beneficial effects against Alzheimer’s disease. The author suggested that further randomized control trials are needed for validation of the results, along with other recommendations, so that it can be conclusively stated that PC can systematically reduce the effects of Alzheimer disease (42). Again, these conclusions highlight the need for studies abridging suitable populations, adequate control trials, and proper statistical data processing, so that generalizations can be made.

4.Cancer Protective Effects

Phenolic compounds can inhibit the metastasis of the cellular lines by different mechanisms, including the removal of carcinogenic agents, modulation of cancer cell signaling, and cell cycle progression, promotion of apoptosis, and modulation of enzymatic activities. In addition, they have anti-inflammatory effects and can modulate apoptotic processes in the vascular endothelium. PC are protective and responsible for lowering tumor growth. This type of beneficial effect was observed for various cancer sites, including the mammary glands, skin, lung, and liver, and some sites of the digestive tract such as the intestine, stomach, and mouth. Polyphenolic compounds provide chemoprevention by several identified mechanisms, such as oxidation prevention, antiproliferation, detoxification of enzymes, initiation of apoptosis or cell cycle arrest, host immune system regulation, estrogenic/antiestrogenic activity, and anti-inflammatory activity by producing alterations in cellular signaling (6,12,30). Additionally, there is increasing evidence suggesting that polyphenols are more bioavailable when considering their metabolites. In addition, this raises the question of whether host metabolites and microbial catabolites of polyphenolic compounds can retain some biological activities. In two recent reviews, the role of dietary PC in cancer management was addressed (41,42)

5.Antidiabetic Effects

Phenolic compounds have an effect on the prevention and management of type 2 diabetes. The potential of PC as antidiabetic agents may be due to its inhibitory action in the gut for glucose absorption, promotion of glucose uptake in peripheral tissue uptake, stimulation of insulin and glucagon-like peptide 1 secretion, and suppression of glucose release from liver (43). Moreover, it is suggested that PC may inhibit aldose reductase, α-amylase, and α-glucosidase (44), claim that seems to be supported by recent findings (43,45). Again, the antidiabetic effect of dietary polyphenols is the subject of some controversy. As reviewed in detail recently (44), some epidemiological research suggests that dietary polyphenols might control and prevent T2D, e.g., PC from grape pomace (46), but opposite opinions have been unveiled (47,48). Such discrepancies have been related to major variation between different populations and measurement errors in dietary intake (23,38).

6.Cardiovascular Effects

Cardiovascular diseases, including coronary artery diseases, stroke, heart failure, and hypertension, are the first cause of death globally (24). Many naturally occurring compounds and foods are promoted for the prevention of such diseases;

studies have demonstrated that consumption of PC reduces the risk of major cardiovascular events. A broad range of epidemiological studies and human trials have shown that a diet rich in polyphenols, based on balanced consumption of tea, vegetables, fruits, and cocoa, increases the likelihood of cardiac safety (38,22). For instance, epidemiological studies summarized in a meta-analysis have suggested that there was an 11% reduction in the risk of cardiovascular disease by having 3 cups of tea per day (49). In addition, it has been proposed that the antioxidant properties of polyphenols might protect vascular endothelial function against the deleterious consequences of the oxidation of low-density lipoproteins (LDLs), as oxidized LDL can impair endothelium-dependent vasorelaxation. PC play a meaningful role in reducing cardiovascular diseases through an improvement in vascular function and a modulation of inflammation (34,5).

7. Obesity

Numerous clinical interventions have investigated the effects of polyphenol-rich intake on anthropometric variables, namely weight, body mass index (BMI), waist circumference, and body fat mass. Clearly, clinical studies pointed towards significant beneficial effects; the studies confirmed a significant reduction in body weight, BMI, waist circumference, and body fat mass in men who took a green tea extract compared with the control group. There are several potential mechanisms whereby polyphenols may influence body weight and composition. According to the prevailing hypothesis, polyphenols enhance energy expenditure, affect sympathetic nervous system activity, and stimulate the oxidation of fat (13,27). The anti-obesity role of dietary polyphenols has been reviewed recently (50, 37), where the contribution of several foods is highlighted through several studies. The most significant foods for said role were: green tea extracts, rich in EGCG, epicatechin, epigallocatechin, and epicatechin-gallate; berries, rich in anthocyanins; onions, rich in quercetin; and soybeans, rich in isoflavones. In a recent work, involving the intake of PC-rich foods by Iranian women, significant negative associations were observed between: stilbenes and lignans intake and BMI; beverages containing phenolic acids and hip circumference; total polyphenols intake and weight-to-hip ratio; stilbenes intake and cholesterol level (24). Again, it should be highlighted that some results in the literature are conflicting, and ascribe this to disparate study designs and lengths, variation of population and diversity of the dietary polyphenols used (20).

8. Antimicrobial Activity

Polyphenols have been demonstrated to have potential antibacterial, antifungal, and antiviral activities (9). Indirectly, they affect the growth of some Gram-negative bacteria, such as Escherichia coli and Pseudomonas fluorescens (18). EGCG, extracted from green tea, was shown to bind directly to the peptidoglycan from Staphylococcus aureus, impairing cell integrity and destroying the osmotic protection of the cell wall. Moreover, EGCG inhibited penicillinase activity (14). Antimicrobial activity has also been ascribed to flavonoids (Figure 1), and the structures of flavonoids having properties of antifungal, antiviral, and antibacterial activity have been isolated and identified (6).

Green tea leaves, rich in EGCG, exhibited a minimum inhibitory concentration (MIC) of 125 µg/mL in the case of multidrug-resistant (MDR) E. coli, MDR S. aureus and their reference strains (11). The antimicrobial role of green tea against MDR E. coli was further reinforced in a more recent work (10). Curiously, the size of green tea particles was shown to be a key parameter for their antimicrobial activity, which was absent for those exceeding nano sizes. The authors also noticed that EGCG correlated positively with an antibacterial effect against oral microflora (7). In another study, juices from cranberry, Japanese quince, and sea buckthorn displayed antimicrobial activity against several Gram-positive and Gram-negative bacteria, which was associated with their high content of PC. Wild rose, chokeberry, both rich in flavonoids, and elderberry juices, rich in anthocyanins, displayed activity mostly against antimicrobial activity only against Gram-positive strains tested (safe for Enterococcus faecalis and Clostridium perfringens) (10). Studies have proven antifungal activity against pathogens, such as Aspergillus, Candida, Cladosporium, and Penicillium genera (7). Despite the well-established antimicrobial role played by PC, due to their structural diversity (Figure 1), the mechanisms underlying their activities have not yet been fully resolved (10).

9-Anti-inflammatory Effects:

Polyphenols possess anti-inflammatory properties, which can help reduce chronic inflammation in the body. Chronic inflammation is linked to various diseases, including diabetes, obesity, and certain types of cancer. By reducing inflammation, polyphenols may contribute to overall health and disease prevention (5)(6). Polyphenols have shown promising anti-inflammatory effects in various studies. Here are some ways in which polyphenols can exert their anti-inflammatory actions: Modulation of Inflammatory Mediators: Polyphenols can inhibit the production and activity of pro-inflammatory mediators, such as cytokines (e.g., tumor necrosis factor-alpha, interleukins), prostaglandins, and nitric oxide. They can downregulate the expression of genes involved in inflammation, thereby reducing inflammation at the cellular level (1)(2). Modulation of Inflammatory Signaling Pathways: Polyphenols can interfere with signaling pathways involved in inflammation, such as nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinases (MAPKs). They can inhibit the activation of these pathways, leading to reduced production of inflammatory molecules (5)(6). It's important to note that the anti-inflammatory effects of polyphenols can vary depending on factors such as the specific compound, dosage, bioavailability, and individual variations. Further research is needed to fully understand the mechanisms and potential benefits of polyphenols in managing inflammation-related conditions.

Conclusion:

Phenolic compounds abridge a wide diversity of compounds that are vastly distributed in fruits cereals and beverages. They play important roles in human health, mainly the consumption of food rich in PC is related with many human health benefits, mostly due to the antioxidant activity. Several analytical methods have been developed for the identification, quantification, and evaluation of the bioactivity of PC. This has contributed to expanding the range of PC and derived metabolites currently known.

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