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The Impact of Polyphenols on Nutrition and Health

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ABSTRACT

Polyphenols are plant-sourced compounds that exhibit important dietary features on human health. They have been defined and used either as a food source or as a raw material in the food industry to enhance functional properties and nutritional quality. They have significant positive bioactivities as; antioxidant, anti-inflammatory, anti-carcinogenic, cardiovascular health protection, immune supporter, and also benefits on digestion and brain functioning. The effects and bioactivity ranges were studied in the literature which has been discussed in the review to emphasize the importance of these natural compounds to provide insight into health and well-being.

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Polyphenols: Definition, History

Polyphenols are defined as plant-sourced metabolites which exhibits antioxidant characteristic (Galanakis, 2018). Even though polyphenol does not emphasize a strict chemical term it refers to a big class of dietary beneficial chemical groups that include flavonoids, phenolic acids, or tannins and their derivatives (Williamson, 2017). Polyphenols are mentioned to be the most abundant antioxidants in the diet which could be as high as 1 gram in a day. This level of intake is related to an important health outcome. Moreover, these plant-sourced chemicals provide prevention of diseases with those related to oxidative stress (Scalbert et al., 2005).

In the literature, the initial addressing of polyphenol chemicals goes back to the 20th century, especially with the terms like "plant polyphenols" and "vegetable tannins". After the mid-1900s paper chromatography was discovered with various analytical methods to measure numerous chemicals polyphenol-related research shifted gears (Cheynier et al., 2015; Quideau et al., 2011). In 1957 "Plant Phenolic Group" was founded Bate-Smith and Tony Swain who later defined plant polyphenols as "water-soluble phenolic compounds having molecular weights between 500 and 3000 (Da) and, besides giving the usual phenolic reactions, they have special properties such as the ability to precipitate alkaloids, gelatin and other proteins from solution" (Bate-Smith, 1962; Cheynier et al., 2015). This was later updated to the term polyphenol as a descriptor and the molecular mass was altered to be up to 4000 Da (Haslam & Cai, 1994). Later with the efforts of the scientists involved in the field, the polyphenols were defined as plant secondary metabolites which are produced by the shikimate-derived phenylpropanoid and/or the polyketide pathway(s) with at least two phenolic rings and being devoid of any nitrogen-based functional group in the basic structure (Quideau et al., 2011).

Classification of Polyphenols

In light of the mostly accepted definition done by Quideau et. al. (2011), polyphenols are the largest and most broadly distributed group of secondary metabolites (Scalbert & Williamson, 2000). This large classification is mostly the result of the acceptance of the hydroxyl groups on aromatic rings, phenol rings, phenolic acids, or phenolic alcohols in the chemical structure to be categorized as polyphenolic chemicals (Galanakis, 2018). The aforementioned mechanism of secondary metabolite production leads to the formation of phenylpropanoids and simple phenols by the shikimic acid pathway and polyketide pathway, respectively (Sánchez-Moreno, 2002). Generally, plant polyphenols are produced with the shikimic acid pathway while the combination of the shikimic acid pathway and polyketide pathway leads to the production of flavonoids (Galanakis, 2018).

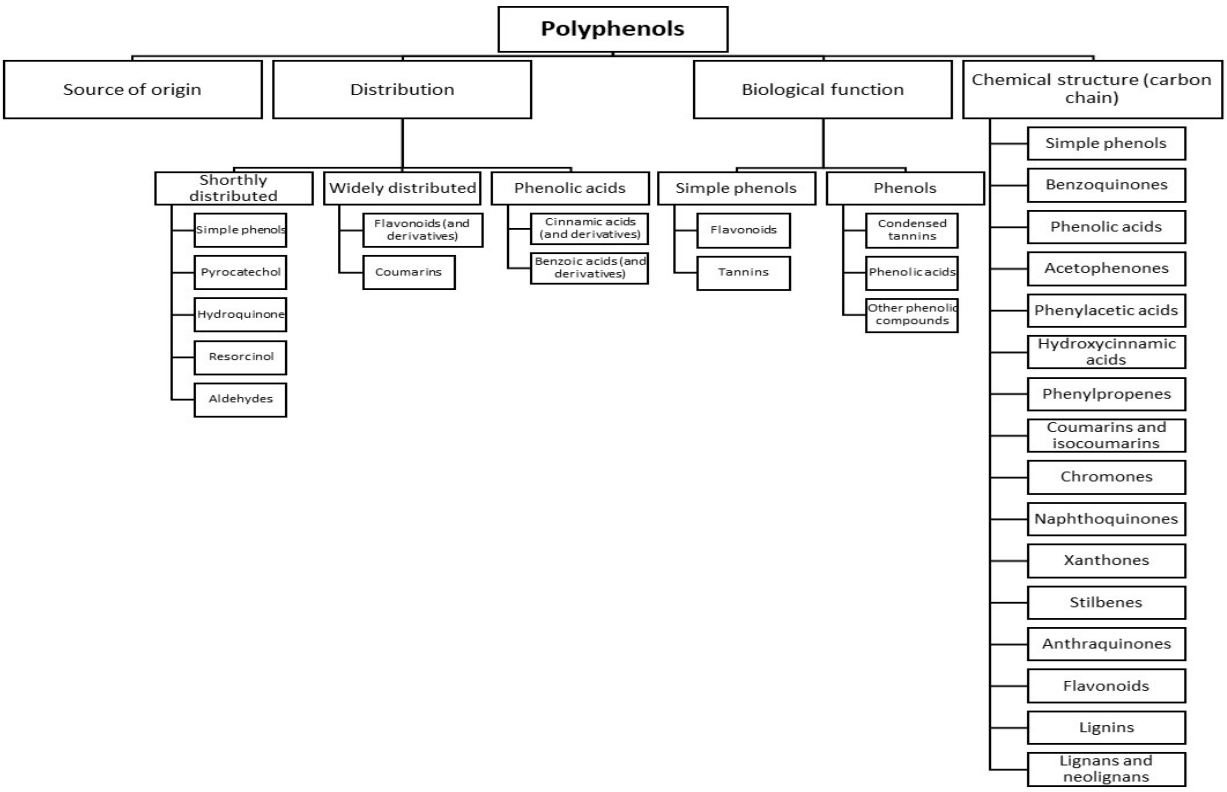

Figure 1. Classes of polyphenols based on various factors (Bravo, 1998; Harborne, 1989; Sánchez-Moreno, 2002)

Therefore, due to the diversity and wide distribution due to the source of origin, distribution, biological function, and chemical structures, polyphenols are categorized. Figure 1 illustrates the main classification methods based on the categorizes.Even though the literature involves several factors to classify those polyphenol groups of chemicals the main classes of polyphenols are flavonoids, phenolic acids, lignans, stilbenes, and others (Galanakis, 2018). Flavonoids refer to a typical chemical structure that involves two benzene rings with phenolic hydroxyl that are connected by three central carbon chains to form the C6-C3-C6 series as a basic chemical skeleton (Chen et al., 2022). The oxidation level of C3 leads to different structures which are named accordingly as; flavonoids, flavonols, isoflavones, anthocyanins, chalcone, nerone, flavane, etc. (Yildiz, 2010). Moreover, flavonoids act as a natural pigment with loads of physiological duties as well as benefits for human and animal health. This important class of polyphenols possesses antioxidant anti-inflammatory, antivirus, anticancer and antibacterial activity (Chen et al., 2020, 2022; He et al., 2006). Polyphenols exhibit antibacterial activity by disrupting bacterial membranes, inhibiting enzymes, and modulating quorum sensing pathways. For instance, studies have demonstrated that olive oil polyphenols shows strong antibacterial effect against Salmonella Typhimurium and S. aureus (Guo et al., 2020). Another literature source suggests polyphenols to be used not only as a food additive for antibacterial effect but also for food packaging systems due to its natural antibacterial activity (Bae et al., 2022). Phenolic acids are the main plant phenolic compound group that has one carboxylic acid group in the chemical structure (Kumar & Goel, 2019). These compounds have two sub-groups hydroxybenzoic and hydroxycinnamic acid and all provide very high antioxidant activity (Clifford, 1999; Tsao & Deng, 2004). The former sub-group is derived from cinnamic acid and is found in the form of ferulic, caffeic, p-coumaric, and sinapic acids whereas the latter hydroxybenzoic acid is derived from benzoic acid and found in the form of p-hydroxybenzoic, protocatechuic, vanillic, and syringic acids (Kumar & Goel, 2019). Lignans on the other hand, are derived from the shikimic acid biosynthetic pathway and they contain a basic scaffold of at least two phenylpropanoid units which are formed monomers of cinnamic acid, cinnamyl alcohol, propenyl benzene, and allyl benzene (Ayres & Loike, 1990; Cui et al., 2020; Teponno et al., 2016). These plant polyphenols exhibit important features as antitumor, antioxidant, antibacterial, immunosuppressive, and anti-asthmatic (Cui et al., 2020). Lastly, stilbenes suppress a smaller portion intake compared to the rest in the mammal diet. Despite the smaller intake, they exhibit important physiological effects such as the anti-carcinogenic effect of resveratrol (Galanakis, 2018).

Food Sources of Polyphenols

A wide variety of fruits and vegetables, such as berries, whole-grain cereals, and cacao, as well as beverages, such as coffee, tea, and wine, have been shown to contain around 800 distinct types of polyphenols. Phenolic compounds are not only widespread in plants that are edible but also in plants that are not edible. These compounds have been shown to have numerous biological impacts, one of which is the ability to act as an antioxidant. The food industry is becoming increasingly interested in the crude extracts of fruits, herbs, vegetables, grains, and other plant materials that are rich in phenolic content (Table 1).

Table 1. Polyphenols in Foods

Polyphenols	Food Sources	References
Flavonoids, Catechins	Green, Black Tea, Grapes, Cocoa, Lentils, Berries	(Dias et al., 2021)
Flavanones	Orange, Grapefruit, Lemon, Tangerine, Olive, Olive Oil	(Yang et al., 2022)
Flavanols	Green vegetables, Apples, Onions, Berries, Olive oil	(Luo et al., 2022)
Anthocyanins	Strawberry, Colorful fruits, Black grapes, Wine, Pink olives	(Qi et al., 2022)
Non-flavonoid polyphenols		
Resveratrol	Grape skin, Red wine, Nuts (almonds, walnuts, etc.)	(Tian & Liu, 2020)
Curcumin	Turmeric, Mustard	(Jiang et al., 2021)
Coumarin	Strawberry, Blueberry, Apricot, Cherry, Cinnamon, Licorice root	(Lončar et al., 2020)
Phenolic Acids		
Ellagic acid	Walnut, Strawberry, Blueberry, Pomegranate, Grape	(Lorenzo et al., 2019)
Tannic acid	Nettle, Tea, Berry fruits, Olive, Olive oil	(Dai et al., 2022)
Gallic acid	Tea, Mango, Strawberry, Soy, Olive, Olive oil	(Parveen et al., 2019)
Caffeic acid	Blueberry, Kiwi, Plum, Cherry, Apple	(Maity et al., 2022)

This is due to the fact that these extracts retard the oxidative destruction of lipids and, as a result, increase the quality of food as well as its nutritional content (El Gharras, 2009).

Biological Activities and Health Effects of Polyphenols

Nutrition today seeks the attention of many researchers from diverse fields such as epidemiology, biochemistry, health sciences, chemistry, psychology, food engineering, pharmacology, biology, chemistry, etc. As a well-known fact food is essential for energy yet modern-era human societies replaced food to be something more than this. Food is expected to promote energy as well as have a positive impact on health (functional foods) or also promote potentially healthier aging and well-being. Amongst these beneficial expectations, one can advise to include or increase the intake of polyphenols because of their popular effects on health. This benefit is a fact but still, the biochemical interactions, metabolic pathways, enzyme actions, and cellular regulations are being investigated to confirm the potential effect of polyphenols on human health (Williamson, 2017).

The type of polyphenol and free radicals on the other hand is critically important for the health affect. Despite the fact that polyphenols having important advantages in general, free radicals and specific types of it should be specified. For instance, cardiovascular effect of polyphenols is usually associated with flavonols. Clinical studies have shown that cocoa flavanols improve endothelial function and reduce blood pressure in hypertensive patients (Schroeter et al., 2006). These findings support the cardiovascular benefits of polyphenols.

Polyphenols are micronutrients that are essential for facilitating biochemical operations in the body. These plant-based foods may have been used reversibly instead as plant secondary metabolites, phytochemicals, phytonutrients, antioxidants, bioactive chemicals, etc. (Hertog et al., 1995). Polyphenols' bioactivities will be outlined in this article as their properties of; antioxidant, anti-inflammatory, anti-carcinogenic, and cardiovascular health.

Antioxidant Activity

Polyphenols are the secondary metabolites of plants that are secreted to protect the plant against environmental stress such as UV light, climate, pests, and insects. Until the 1990s they were classified as general antioxidants due to their biological activities in plants and potentially in humans with the diet (Serafini et al., 1994). So far the researchers made loads of contributions with the investigations according to food type, health condition, age/gender/status-related alterations in-vivo and in vitro. Polyphenols exhibit free radical scavenging activity primarily through their hydroxyl groups, which donate electrons to neutralize reactive oxygen species (ROS). For example, catechins from green tea have demonstrated high efficacy in scavenging hydroxyl radicals and superoxide anions (Rice-Evans et al., 1997). This mechanism plays a crucial role in preventing oxidative damage to lipids, proteins, and DNA.

Generally, antioxidant activity is related to the phenolic chemical structure with the catechol-like moieties and delocalized unpaired electrons in the structure (Croft, 2016). Dietary polyphenols show reasonable antioxidant activities either in vitro or in vivo. An in-vitro study demonstrated that catechins from green tea scavenge superoxide anions and hydroxyl radicals, protecting lipid membranes from peroxidation (Rice-Evans et al., 1997). The literature presents numerous studies in the antioxidant activities including, scavenging of free radicals, lipid oxidation, hydroperoxide formation process, etc. Not only in the plants to protect them against natural stress sources but also in dietary usage polyphenols' antioxidant character has an impact on plasma, membrane, transcription factors, and enzyme activities. Moreover, other beneficial features such as anti-inflammatory, anti-carcinogenic, neuroprotective, cardiovascular health, and anti-diabetic are somehow related to the antioxidant characteristics either directly or indirectly.

Antioxidant polyphenols are a common food preservation compound in the industry. They are used for three main purposes;

- Food additives, as an antioxidant compound, provide longer shelf life,

- As a packaging material, designed packaging materials with supported antioxidant behavior to provide better protection,
- Processing aid is used to provide an easier process that makes it less susceptible to environmental effects.

Some typical examples of literature studies can be listed as; lipid oxidation blockers in; fish oil (Luther et al., 2007), in fish (Ramanathan & Das, 1992), meat (Chamorro et al., 2015), muscle food (Wu et al., 2022); polyphenol supported packaging (Cheng et al., 2022; Liu et al., 2019; Roman et al., 2016), processing aids (Aguilar et al., 2008; Aliakbarian et al., 2008; Ranalli & De Mattia, 1997).

Anti-inflammatory Activity

Inflammation is a biological response to some agents like pathogens, irritants, or damaged cells which are associated with diseases and certain health issues like rheumatoid arthritis, atherosclerosis, asthma, obesity, diabetes, coronary heart diseases, and aging (de Cássia da Silveira e Sá et al., 2013; Li et al., 2014). Human biology tries to suppress the inflammation to "treat" the disorders to become "healthier" status. Polyphenols show significant activity in terms of inflammation suppression as an anti-inflammatory in vivo and in vitro (Yahfoufi et al., 2018). In a murine model, quercetin reduced inflammation by downregulating TNF-α and IL-1β expression, showcasing its potential as a natural anti-inflammatory agent (Xu et al., 2019).

Literature provides a good insight into polyphenols' anti-inflammatory effects. Some examples are; olive polyphenols (Bucciantini et al., 2021), fruit polyphenols (Joseph et al., 2016), p-coumaric acid (Pragasam et al., 2013), black seeds (Ghannadi et al., 2005), green tea (Cavet et al., 2011; Lambert et al., 2010; Tipoe et al., 2007).

Anti-inflammatory activity is triggered by the antioxidant capacity. Hence, it will be clear to see these effects at once in the polyphenols (Kulkarni et al., 2008; Zhang & Tsao, 2016). Good evidence for such a synergistic effect is curcumin which has a great advantage for the bioactivity of polyphenols especially as an anti-inflammatory and antioxidant (Arshad et al., 2017; Menon & Sudheer, 2007; Motterlini et al., 2000).

Anti-carcinogenic Activity

Cancer is one of the top death-causing diseases globally and most of the nutritional and epidemiological research focuses on the effect of consumed foods on cancer metabolism. The literature is clear that polyphenols play a significant role in the prevention of cancer which has been proven especially in signaling pathways for carcinogenesis (Keskin, 2023, 2024; Keskin et al., 2023), skin cancer (Sajadimajd et al., 2020), gastric and stomach cancer (Vitelli-Storelli et al., 2020), colorectal cancer (Ding et al., 2020; Yammine et al., 2021), prostate cancer (Li et al., 2013), liver cancer (Li et al., 2023; Loa et al., 2009), and lung cancer (Sadava et al., 2007; Wang et al., 2011).

Some specific polyphenols have been previously listed by Li et al. (2014) as proanthocyanidins, flavonoids, resveratrol, tannins, epigallocatechin-3-gallate, gallic acid, and anthocyanin. These compounds are considered not as a treatment aid only but also a dietary source to prevent cancer as well. Another important finding in the literature is about resveratrol. Resveratrol, a stilbene found in grapes and red wine, has shown potential in reducing oxidative stress and modulating inflammatory pathways in clinical studies. For instance, a trial involving colorectal cancer patients demonstrated reduced oxidative markers and improved anti-inflammatory cytokine profiles with daily supplementation of resveratrol (Patel et al., 2010). Yet, we have to mention that cancer is still one of the diseases that are hard to treat, especially with complex mechanisms of cellular production (e.g. metastases) that are affected by many factors in the body including genetic factors. Polyphenols were found to affect the enzyme biology that could be showing an anti-carcinogenic effect with the carcinogen bounding capability as well as avoiding excessive cell damage during the cancer metabolism. The polyphenols still have to be tested in vivo and in vitro to be used for therapeutic purposes.

Cardiovascular Health

Polyphenols show a great advantage in cardiovascular health thanks to their antioxidant activities. In the literature, this effect was associated with postprandial hyperlipidemia and oxidative stress which could be reduced by polyphenols (Li et al., 2014). Polyphenols were found to have a significant effect on; atherosclerosis, myocardial infarction, and unstable angina which have very high case reporting globally yet significantly lower in the Mediterranean region due to higher intake of polyphenols (Nadtochiy & Redman, 2011). Moreover, antioxidant and anti-inflammatory effects help to protect heart health in the long term.

Polyphenols were also found to reduce blood pressure which directly reduces the risk factor for the heart and helps the enlargement of the blood veins (Marunaka et al., 2017; Medina-Remon et al., 2013). Additionally, polyphenol-rich diets were found to be associated with the lowering of low-density lipoprotein (LDL) which is linked with high blood pressure (Davalos et al., 2006; Hernáez et al., 2015).

Dietary Intake of Polyphenols

The average consumption of polyphenols through diet is about 1 g/day, ranging from 800-900 mg/day in Finland to 800-1100 mg/day in Spain, depending on diet, gender, and other socioeconomic factors. This intake is 100 times more than that of vitamin E and -carotenes and 10 times greater than that of vitamin C. Polyphenols may be the primary bioactive dietary components involved in redox homeostasis due to their stronger anti-oxidant effects than vitamin E (Tresserra-Rimbau et al. 2018; Landete 2013).

Conclusion

As multipurpose plant-derived substances, polyphenols have shown great promise in enhancing human health due to their wide range of bioactivities, which include cardiovascular protection, anti-inflammatory, anti-cancer, and antioxidant properties. These bioactivities demonstrate the potential of polyphenols in functional foods and nutraceutical uses in addition to aiding in the prevention of disease. Even with a wealth of study, more investigation is necessary to fully realize the therapeutic effects of polyphenols due to the intricacy of their metabolism and

interactions inside the human body. This article offers a strong basis for furthering research in this area and emphasizes the vital role that dietary polyphenols play in promoting a healthy lifestyle. Future research should focus on expanding our knowledge of the molecular processes that underlie polyphenols' beneficial impacts on health. Clarifying their metabolism, bioavailability, and cooperative relationships with other dietary elements should receive particular attention. Furthermore, polyphenols' stability and effectiveness in food and pharmaceutical applications may be improved by utilizing developments in biotechnology and nanotechnology. The key to optimizing polyphenols' public health impact and making sure that their advantages are available to a wide range of communities globally will be to develop creative ways to integrate them into regular diets.

Declarations

This study was presented at the 7th International Anatolian Agriculture, Food, Environment and Biology Congress, (Kastamonu, TARGID 2024)

Author Contribution Statement

Eda Adal: Conceptualization, investigation, visualization, writing-review and editing, supervision, writing original draft

Tuğba Aktar: Conceptualization, investigation, visualization, writing-review and editing, supervision, writing original draft

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Conflict of Interest

The authors declare no conflict of interest.

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