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Polyphenols: Food Sources and Health Benefits

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Abstract

The current scientific knowledge on the relationship between diet and human health is greatly focused on the effects of phytochemicals, especially polyphenols, on chronic diseases, due to their preventive effect as shown by many epidemiological studies. Herbs, cocoa products, and darkly colored berries, such as black elderberries, chokeberries, and black currants, are the richest dietary sources that contribute to the average intake of polyphenols of about 1 g/day. Polyphenols that are the most common in the human diet are not necessarily the most active in the body because their beneficial effects depend on the plant matrix in which they are incorporated and on processing methods and endogenous factors such as microbiota and digestive enzymes. Polyphenol-rich foods are considered as being potential functional foods due to antioxidant, anti-inflammatory, antimicrobial, immunomodulatory, anticancer, vasodilating, and prebiotic-like properties. This review will outline findings on the preventive effects of polyphenols on chronic diseases, the factors affecting polyphenol bioavailability and bioaccessibility, and new trends in functional food production.

Keywords: polyphenols, dietary intake, chronic diseases, bioavailability, functional food

1. Introduction

Polyphenols are the most common phytochemicals in human diet and comprise a variety of compounds with a great diversity of structures, ranging from simple molecules to polymers with high molecular weight. Polyphenols are plant secondary metabolites present in all plant tissues, and their primary role is to protect plants from insects, ultraviolet radiation, and microbial infections and to attract pollinators [1]. According to the chemical structures of aglycones, polyphenols are classified as flavonoids, phenolic acids, lignans, and stilbenes [2]. Fruits, vegetables, whole grains, chocolate, and drinks like tea and wine are good sources of polyphenols,

but due to diverse chemical structures, it is difficult to estimate the total polyphenol content in foods. Beneficial health effects of these phytochemicals are directly linked to regular daily intake and bioavailability. The aim of this review is to present current knowledge regarding evidence on chronic disease prevention, factors affecting polyphenol bioavailability and bioaccessibility, and new trends in the production of polyphenol-enriched functional foods.

2. Classification and food sources of polyphenols

Dietary polyphenols comprise a variety of compounds among which flavonoids and several classes of non-flavonoids are usually distinguished. In nature, polyphenols are bound to sugars in the form of glycosides. However, classification of polyphenols in this review will be presented according to the chemical structures of aglycones. These compounds contain at least one aromatic ring and are classified into different groups according to the number of aromatic rings and the structural elements that bind these rings together. Therefore, polyphenols are classified as flavonoids, phenolic acids, lignans, and stilbenes [2].

Flavonoids are the largest group of phenolic compounds and are widely distributed in plants, especially in fruits. Their structures consist of two aromatic rings that are bound together with a three-carbon bridge that form an oxygenated heterocycle (**Figure 1**). Their biological activities, including antioxidant activity, depend considerably on both structural difference

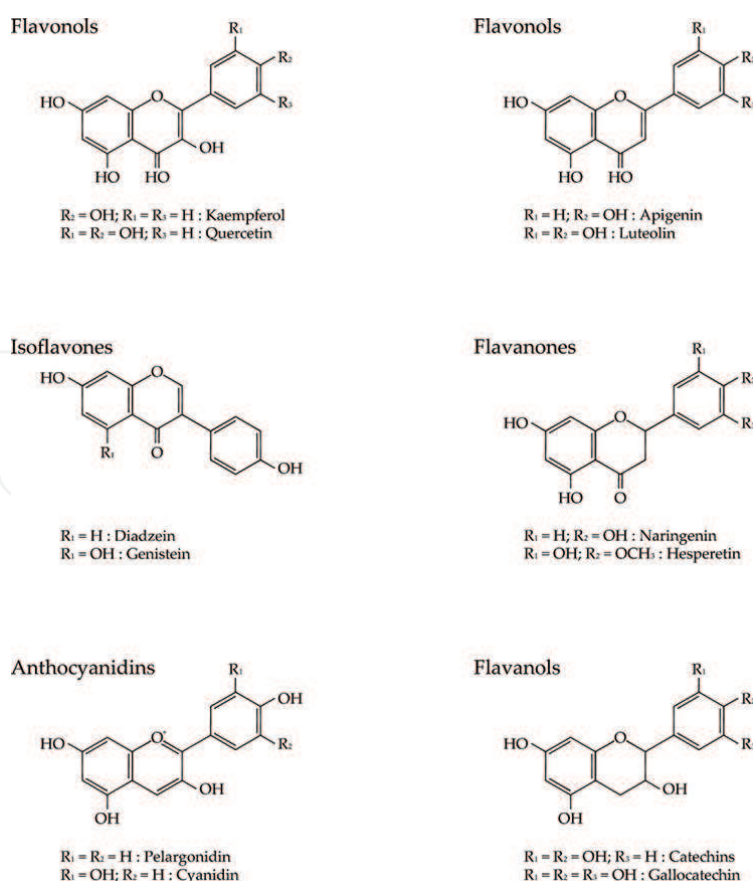


Figure 1. Chemical structures of flavonoids [2].

and glycosylation patterns [3]. According to the degree of oxidation of the central ring and the number and position of –OH groups, flavonoids can be divided in six subclasses: flavonols, flavones, isoflavones, flavanones, anthocyanidins, and flavanols.

Flavonols are one of the most ubiquitous flavonoids in food, and their main representatives are quercetin and kaempferol, typically found as glycosides [2]. Data on the content of flavonols in commonly consumed fruits, vegetables, and drinks can vary significantly due to local growing conditions (microclimate and agrotechnical requirements), seasonal changes, and varietal differences. The most significant dietary sources of this group of flavonoids are yellow and red onion and spinach, but the richest sources are capers, saffron, and dried Mexican oregano (**Table 1**).

The most common *flavones*, such as apigenin and luteolin, are not widely distributed in the plant kingdom although significant amounts are found in celery, parsley, and some herbs (**Table 1**). Tangeretin and nobiletin are polymethoxylated flavones, occurring only in tissues and peels of citrus fruits such as tangerine, grapefruit, and orange. These flavones have methylated hydroxyl groups, which increase their metabolic stability and improve oral bioavailability [4].

The best sources of *isoflavones* are legumes, especially soybeans, and their processed products containing significant amounts of daidzein and genistein (**Table 1**). Although the fermentation of soybeans during the manufacturing of certain foods, such as miso and tempeh, does not cause the loss of isoflavones, they are, however, in the form of aglycones due to bacterial hydrolysis of glycosides [2]. Unlike fermentation, the use of high temperature (the production of soy milk or tofu) can significantly reduce the concentration of isoflavones. Isoflavones possess pseudohormonal properties because of their structural similarity to estrogen, and they are consequently classified as phytoestrogens. Due to their ability to bind to estrogen receptors, soy foods and isoflavone supplements can be potential alternatives to conventional hormone therapy [5].

The most important *flavanones* in food are naringenin and hesperetin. The highest concentrations are found in dried herbs and citrus fruits (**Table 1**), and their glycosides are responsible for the bitter taste of grapefruit and some varieties of oranges.

Anthocyanidins are a subgroup of flavonoids that provide color to plant tissues (flowers, leaves, fruits, and roots), ranging from blue, purple, and red, depending on the pH and their structural composition. Anthocyanidins are considered the most important group of flavonoids in plants, having more than 600 compounds identified in nature [6]. They are widely distributed in colored fruits like berries, plums, and cherries as well as in many dark colored vegetables such as red cabbage, eggplant, red onion, and red radish, while the food content is generally proportional to color intensity. The most common anthocyanidin aglycones are pelargonidin, delphinidin, peonidin, petunidin, malvidin, and cyanidin, which is the most widespread in fruits and vegetables. Being highly unstable in the aglycone form, they are in the form of glycosides (anthocyanins) in plants, enabling them to be resistant to light, pH, and oxidation process [2].

Flavanols are the most complex subclass of flavonoids, ranging from simple monomers (catechin and its isomer epicatechin) to oligomers and polymers (proanthocyanidins) and other derived compounds (e.g., theaflavins and thearubigins) [7]. Catechins and epicatechin are

Flavonoid subgroup	Food source	Content (mg/100 g)
Flavonols	Capers	654.71
	Saffron	509.99
	Mexican oregano (dried)	272.07
	Red onion (raw)	128.51
	Spinach (raw)	119.27
Flavones	Celery seed	2094.00
	Peppermint (dried)	1486.29
	Common verbena (fresh)	790.00
	Mexican oregano (dried)	733.77
	Celery leaves (fresh)	133.38
Isoflavones	Soy (flour)	466.99
	Soy paste (cheonggukang)	264.40
	Soybean (roasted)	246.95
	Soy (tempeh)	147.72
	Soy paste (nato)	103.90
Flavanones	Peppermint (dried)	8739.98
	Mexican oregano (dried)	1049.67
	Grapefruit/pummelo hybrid (pure juice)	67.08
	Orange (juice from concentrate)	61.29
	Rosemary (fresh)	55.05
Anthocyanidins	Black elderberry	1316.65
	Black chokeberry	878.12
	Black currant (raw)	592.23
	Lowbush blueberry (raw)	187.23
	Blackberry (raw)	172.59
Flavanols	Cocoa (powder)	511.62
	Chocolate (dark)	212.36
	Broad bean pod (raw)	154.45
	Black tea (infusion)	73.30
	Green tea (infusion)	71.17

Table 1. The richest food sources of flavonoid groups determined by liquid chromatography [8].

found in many types of fruits such as strawberry, apple, and peach, but cocoa products and black and green tea are the richest sources (**Table 1**). In contrast to other classes of flavonoids, flavanols are stable and are not glycosylated in foods. The production of black tea decreases

the concentration of catechins, mainly due to the action of polyphenol oxidase during fermentation, but at the same time, theaflavins and thearubigins are accumulating agents [1]. The oligomers and polymers of flavanols are also referred to as condensed tannins or proanthocyanidins that mainly consist of (epi)catechin units called procyanidins. They are responsible for the astringent character of some fruits and beverages and for the bitterness of chocolate [2].

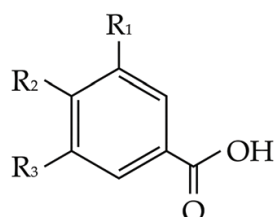
Phenolic acids can be divided into two main groups—benzoic and cinnamic acids and their derivatives (**Figure 2**). The most important derivatives of benzoic acids are gallic and ellagic acid, which are found in various types of fruit such as raspberries, cranberries, and pomegranates and in nuts (e.g., chestnut contains 1215.22 mg of hydroxybenzoic acids per 100 g). Hydroxybenzoic acids are also components of complex structures like hydrolyzable tannins (gallotannins in mangoes and ellagitannins in red fruit such as strawberries and raspberries) [2].

The most important derivatives of cinnamic acids are coumaric, caffeic, ferulic, and sinapic acids. In food, they are often in the bound form and can only be released upon acid or alkaline hydrolysis or by enzymes. Caffeic acid is the most abundant phenolic acid and represents about 87% of the total hydroxycinnamic acid content of most fruits [2]. Caffeic and quinic acid together form chlorogenic acid, which makes up about 10% of green Robusta coffee beans. Regular consumption of coffee may provide more than 1 g of chlorogenic acid, which means that for many people it is the main source of dietary polyphenol [1].

Lignans are formed with two phenylpropane units and a four-carbon bridge, leading to many different chemical structures in nature (**Figure 3**). The highest amount of these compounds is found in flaxseeds, and other valuable sources are grains and certain vegetables. Lignans are one of the major classes of phytoestrogens, together with isoflavones mentioned earlier. In plants, they are typically found as glycosides and are converted by intestinal bacteria to give metabolites with estrogen activity like equol, enterodiol, and enterolactone [9].

Stilbenes are phytoalexins produced by plants in response to injury and infections. They are present in human diet in low quantities, and only resveratrol is considered important to human health (**Figure 4**). The most important dietary source of resveratrol is grapes and red wine. Resveratrol is directly linked to the *French paradox*, in which it was observed that the French consume significant amounts of saturated fatty acids while rarely suffering from cardiovascular disease and having a lower mortality rate compared with populations from other European countries. It is believed that their regular consumption of red wine plays a key role in preventing heart disease [10].

Hydroxybenzoic acids



Hydroxycinnamic acids

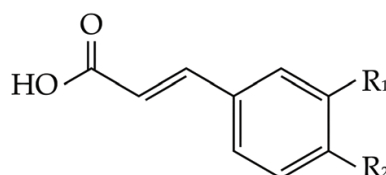


Figure 2. Chemical structure of phenolic acids [2].

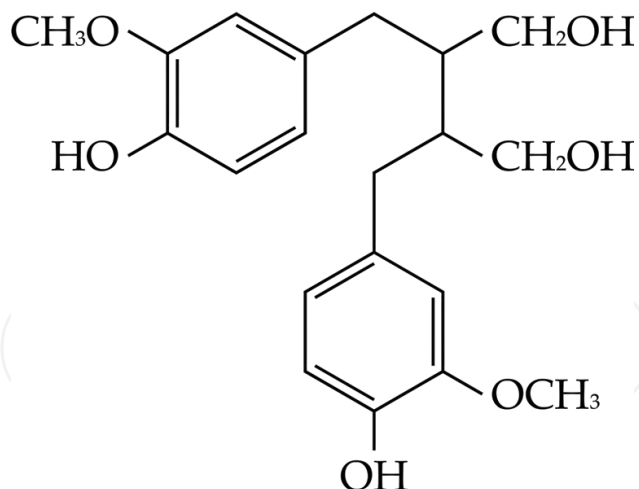


Figure 3. Chemical structure of lignans [2].

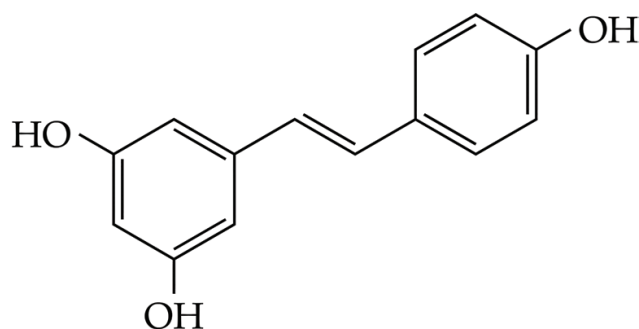


Figure 4. Chemical structure of stilbenes [2].

3. Health benefits

Polyphenols are the most common phytochemicals in human diet and are in the focus of scientific research due to their biological properties, bioavailability, and bioaccessibility, as well as their effects on the prevention of chronic diseases. Epidemiological studies confirm that moderate and prolonged intake of foods rich in polyphenols could prevent the formation of cancer and chronic diseases such as cardiovascular disease, neurodegenerative disease, type 2 diabetes, and obesity, which are the most common in Western populations [1].

A large primary prevention trial tested the long-term effects of the Mediterranean diet, containing polyphenol-rich foods, on the incidence of cardiovascular disease in participants with high risk but free of cardiovascular disease at baseline (the PREDIMED study). Data on their dietary habits were collected with a validated food frequency questionnaire, and the polyphenol content in foods was obtained from the Phenol-Explorer database. Results showed a significant reduction of cardiovascular events and cardiovascular mortality with a higher intake of total polyphenols, especially flavanols, lignans, and hydroxybenzoic acids [11]. The aim of this study was also to investigate the effect of polyphenol intake on all-cause mortality. Among high-risk subjects, those

with higher polyphenol intake showed a 37% lower mortality risk, compared with those with lower intake. Subgroups of polyphenols with the strongest inverse association were stilbenes and lignans, while flavonoids and phenolic acids had no significant effect on mortality reduction [12]. However, the European Prospective Investigation into Cancer and Nutrition (EPIC) reported that higher flavonoid intake in the diet was associated with a 29% reduction in all-cause mortality, in particular for the subclasses of flavanones and flavonols, which decreased the incidence of cardiovascular disease by 40 and 41%, respectively [13]. Although a beneficial effect has been proven, more controlled trials are needed to definitively clarify the benefits of different polyphenol subgroups and to define minimum levels of dietary intake. Beneficial effects of polyphenols on cardiovascular disease have been attributed to their antioxidant activities, but recent evidence suggests that vasodilatory, anti-inflammatory, and anti-atherogenic properties may also contribute to cardiovascular risk reduction, indicate their ability to improve lipid profile, and modulate apoptotic processes in the vascular endothelium [14].

Growing evidence also indicates that polyphenols may prevent neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease by decreasing inflammatory stress signaling, leading to the expression of genes that encode antioxidant enzymes and cytoprotective proteins [15]. A study conducted by Schmidt et al. [16] showed that green tea extracts can increase the number of connections between neurons of frontal and parietal brain regions which positively correlated with the improvement in the task performance. A double-blind study included 12 healthy volunteers who received either a milk solution with 27.5 g of green tea extract or a milk solution without the extract. The effect of green tea extract on working memory was visualized with functional magnetic resonance imaging (MRI) while performing memory test. Another intervention study confirmed the beneficial effect of blueberries. During 12 weeks of blueberry juice consumption, cognitive function (paired associate learning and word list recall) was significantly improved in older patients with early symptoms of dementia. In addition, symptoms of depression and blood glucose levels were reduced [17].

Many studies investigated the impact of polyphenols on carbohydrate metabolism and possible prevention of diabetes type 2. Polyphenols have the potential to inhibit key enzymes that are responsible for the digestion of dietary carbohydrates (α -amylase and α -glucosidase) and thus modify the postprandial glycemic response [18]. In vitro studies have shown that polyphenol-rich extracts from berries are effective in the inhibition of α -amylase and α -glucosidase at low levels. Tannin-like components (ellagitannins and proanthocyanidins) from raspberry and rowanberry were the most effective for amylase inhibition. A rowanberry fraction rich in proanthocyanidins was as equally strong an inhibitor as the whole rowanberry extract for α -amylase inhibition but was considerably less effective for α -glucosidase inhibition which suggests that tannins are poor inhibitors of α -glucosidase. Among the tested berry extracts, black currants rich in anthocyanins and flavonols had the strongest inhibitory effect on α -glucosidase [19]. The aim of an interesting study conducted by Yang and Kong [20, 21] was to investigate the effect of green tea polyphenols and green, black, and oolong tea extracts on α -amylase and α -glucosidase activity. All tested samples showed a strong inhibitory effect on α -glucosidase, and their inhibitory potency is mainly attributed to tea polyphenols. In contrast, all three types of tea extract significantly enhanced α -amylase activity, whereas green tea showed the highest activation effect. Green tea polyphenols significantly increased α -amylase

activity in low concentrations. A high concentration, however, resulted in a mild inhibitory effect, suggesting that other constituents in the tea counteract the inhibitory effect of polyphenols. A large prospective EPIC-InterAct study examined the association between dietary flavonoid and lignan intake and the risk of developing diabetes type 2 in eight European countries. High intake of flavonoids was associated with a significant risk reduction, while the intake of lignans had no effect. Among flavonoid subclasses, flavonols and flavanols were associated with a significantly reduced risk of diabetes [22]. A comprehensive review by Kim et al. [18] summarizes epidemiological and clinical studies that investigated the relationship between food rich in polyphenols and risk of diabetes type 2. Despite promising data from in vitro and animal studies, the number of intervention surveys conducted on human beings is small. Most studies showed that polyphenols were associated with a lower risk of diabetes type 2, but this association was not entirely consistent. Potential mechanisms of the action of polyphenols in preventing diabetes type 2 include the stimulation of insulin secretion and protection of pancreatic β -cells against glucose toxicity, in addition to the inhibition of salivary and pancreatic α -amylase and α -glucosidase.

Obesity is considered one of the most serious health problems that have assumed the character of a global epidemic. According to the data published by Eurostat in 2014, 51.6% of adults in the European Union are overweight (35.7% pre-obese and 15.9% obese). The in vitro and some in vivo studies suggested that consumption of particular polyphenols (such as catechin in green tea, anthocyanins in blueberries, resveratrol in wine, and curcumin in turmeric) may facilitate weight loss and prevent weight gain due to changes in lipid and energy metabolism [23]. A survey conducted by Basu et al. [24] showed that using a freeze-dried blueberry beverage in obese people with metabolic syndrome for 8 weeks decreased blood pressure and the concentrations of oxidized LDL cholesterol and products of lipid peroxidation. Some researchers suggested that polyphenols may inhibit lipase activity and consequently reduce lipid absorption [25, 26]. Uchiyama et al. [27] have shown that black tea polyphenols in rats with diet-induced obesity can inhibit intestinal lipase activity and suppress the increase of triglyceride levels.

The cause of the aforementioned chronic disease can be associated with oxidative stress resulting from reactive oxygen and nitrogen species. Many in vitro studies have demonstrated that polyphenols can decrease inflammatory markers, reduce oxidative stress, and improve cancer biomarkers, but intervention studies have not always confirmed these positive effects. The reasons which could explain these differences include different doses of administered compounds, polyphenol instability in food and in the gastrointestinal system, a synergistic effect with other antioxidants from the whole food, differences in bioavailability as a result of release from the food matrix, and the presence of food components in the matrix which may enhance or reduce polyphenol bioavailability [28].

4. Dietary intake

The beneficial effects of polyphenols on human health depend considerably on dietary intake. Due to the great diversity of their chemical structures, it is difficult to estimate the

total polyphenol content in foods. Hence, a comprehensive database was developed to help estimate the polyphenol content in certain foods and has been available online since 2009 [8]. Data summarized there were derived from more than 1300 scientific publications. According to this database, Pérez-Jiménez et al. [29] established a list of the 100 richest dietary sources of polyphenols per 100 g of food and in a food serving, using common serving sizes. Data on the total content of polyphenols were calculated based on the sum of all individual polyphenol contents determined by chromatography. In addition, the results were compared with data obtained by the Folin-Ciocalteu method, one of the most commonly used method for estimating total phenolic content. The results showed that the richest sources per 100 g of foods are various herbs and cocoa products (as shown in **Table 1**), while at the top of the list, expressed per serving size, are various darkly colored berries such as black elderberry, chokeberry, black currant, and blueberry. Comparison of the data obtained by different methods showed that the values obtained by the Folin-Ciocalteu method systematically exceed the total amount of polyphenols because this method is not specific and interference with other antioxidants present in the food is possible.

With the aim of estimating polyphenol intake, a large European cohort study was recently conducted in ten countries on more than 36,000 subjects. The results showed that the largest intake of phenolic compounds is in Denmark (1706 mg/day), while the lowest is in Greece (664 mg/day). Similar findings were observed after comparison of intake according to regions; the total polyphenol intake in the non-Mediterranean countries was higher compared with the Mediterranean countries. The most significant sources of phenolic compounds are coffee, tea, and fruit, with phenolic acids contributing to the total intake with more than 50% [30]. This was the first study that applied retention factors from the Phenol-Explorer database to assess the effects of cooking and processing on polyphenol contents in foods. Although the usual cooking of common plant foods causes substantial losses of polyphenols, in this study it did not have a high impact on the estimated total polyphenol intake because vegetables and legumes were not major contributors to polyphenol intake [31].

Research on the dietary intake of phenolic compounds has been conducted also in certain European countries, and the results show that the average intake in France is 1193 mg/day [32], in Poland 1756.5 mg/day [33], and in Spain 820 mg/day [34]. The main dietary sources of the total polyphenols in Spain and France are fruits and nonalcoholic beverages (principally coffee and tea). In Spain, fruits accounted for 44% of the total polyphenol intake and nonalcoholic beverages for 23%, whereas in France fruit accounted for only 17% and nonalcoholic beverages for 55% of the total polyphenol intake. Considering individual foods, the main source of total dietary polyphenols is coffee with 18 and 44% of contribution in Spain and France, respectively. In Spain, in contrast to other countries, olives and olive oils are important sources of polyphenols, accounting for 11% of the total polyphenol intake. Nonalcoholic beverages were the main food contributors to polyphenol intake in Poland and accounted for fully 67% of the total polyphenol intake due to high consumption of coffee and tea. The third main contributor to total polyphenol intake is chocolate, whereas fruits accounted for a lower percentage of intake.

5. Bioavailability and bioaccessibility

The beneficial effects of phenolic compounds on health depend not only on food sources but also on their stability, which can vary depending on the method of raw material processing, the matrix in which they are incorporated, and endogenous factors such as microbiota and digestive enzymes. The fraction of the phenolic compounds that can be released from the food matrix by digestive enzymes or intestinal bacterial flora in the colon is bioaccessible and, therefore, potentially bioavailable for absorption [28]. The FDA has defined bioavailability as the rate and extent to which the active substances or therapeutic moieties contained in a drug are absorbed and become available at the site of the action [35].

Understanding the effects of food processing on polyphenol content and bioavailability is important since most of the food consumed on a daily basis is in a processed form. Conventional methods of thermal processing, such as pasteurization that is still most commonly used, provide microbiological stability and extend shelf life but also cause some undesirable changes such as degradation of polyphenols and other bioactive compounds. The possibility of ensuring food safety and at the same time preserving biologically active compounds has resulted in increased interest in the minimal processing of foods using nonthermal methods, such as high-pressure processing and ultrasound. Studies have demonstrated that in comparison with high-pressure processing, pasteurization causes more degradation of polyphenol, anthocyanins, vitamin C, and the color of strawberry puree [36]. Treatment with high-intensity ultrasound, due to the cavitation effect, can break down cell walls and facilitate the extraction of bioactive compounds, thus increasing their bioavailability. Additionally, increased antioxidant capacity and monomeric anthocyanin content in red raspberry puree treated with high-intensity ultrasound were achieved by Golmohamadi et al. [37].

Food matrix composition and other food components significantly influence bioaccessibility, uptake, and further metabolism of polyphenols. Before becoming bioavailable, polyphenols must be released from the food matrix and hydrolyzed by intestinal enzymes or microflora to aglycones. In vitro gastrointestinal digestion models are a useful tool for assessing the impact of the food matrix and other endogenous factors on the stability and biological activity of phenolic compounds and can be well correlated with results from human studies and animal models [38]. Simulation of the physiological parameters, such as variation in the enzymes, acid and bile salt excretion, availability of the substrate, and the transit time of food through the stomach and duodenum, is challenging in all in vitro digestion models. Gastric digestion is simulated by pepsin-HCl at pH 2 and small intestinal digestion with pancreatin-bile mixture at pH 7, while the absorption step can be simulated with polarized human colon carcinoma cell line (Caco-2 cells) [39]. Commercial digestive enzymes, collected or extracted from omnivorous animals, are most commonly used, but their role in the simulation of the human digestion process is still questionable. On the other hand, human digestive juices contain a complex mixture of different enzymes, enzyme inhibitors, and bile salts, which together contribute to the digestion process of food; therefore, the use of human digestive juices may represent a great advantage over commercial digestive enzymes [40]. Phenolic acids and flavonoids with small molecular weight such as gallic acid, catechins, and quercetin glucosides

are easily absorbed through the tract, whereas large polyphenols such as proanthocyanidins are poorly absorbed [41]. In most of conducted studies, gastric digestion did not have a significant effect on polyphenol stability. In fact, the majority of polyphenols appear to be released in the stomach. Bouayed et al. [38] observed that approximately 65% of apple total phenolics and flavonoids were released in the stomach and only an additional 10% in the small intestine. Results of the study conducted by Correa-Betanzo et al. [42] showed a high stability of total polyphenols and anthocyanins (7 and 1% of reduction, respectively) during simulated gastric digestion, while intestinal digestion caused a significant decrease of 51 and 83%, respectively, in comparison with the non-digested wild blueberry samples. Similar results were obtained by Bermúdez-Soto et al. [43] who reported a significant reduction of anthocyanins (43%) and flavonols (26%) after intestinal digestion of chokeberry. Mild alkaline intestinal environment was shown to influence all phenolic compounds, especially anthocyanins, and it is generally accepted that their bioavailability is low (<1%). An interesting study was conducted by Czank et al. [44] who proved that bioavailability of anthocyanins has been underestimated. The participants consumed an isotopically labeled anthocyanin tracer (cyanidin-3-glucoside), and the concentration was determined in blood, urine, breath, and feces samples. Results showed a high combined recovery from urine and breathe, which was approximately 12%. To date, a little research has been conducted in investigating polyphenol stability by using human gastrointestinal enzymes. Zorić et al. [45] conducted a study on the stability of rosmarinic acid in an aqueous extract of thyme, lemon balm, and winter savory using human digestive juices of the stomach and small intestine. The results showed lower gastrointestinal stability of rosmarinic acid in comparison with similar studies with commercial digestive enzymes.

In the food matrix, polyphenols are usually mixed with different macromolecules such as proteins, lipids, and carbohydrates. Large polyphenols and those with a high number of hydroxyl groups have a high affinity for proteins, which can result in a complex formation that reduces polyphenol absorption [28]. Food rich in polyphenols, such as coffee or tea, is usually consumed with milk. Studies have shown that interactions between polyphenols and milk proteins, especially casein, can decrease the antioxidant activity of coffee and tea [46]. The effect of milk was confirmed in an intervention study by Serafini et al. [47] whose aim was to determine the total antioxidant capacity and (–)epicatechin content in blood plasma after consumption of plain dark chocolate, dark chocolate with full-fat milk, and milk chocolate. Results have shown that the addition of milk, either during ingestion or in the manufacturing process, caused a significant reduction in total antioxidant activity and absorption of (–)epicatechin in the bloodstream. The explanation was in the formation of a complex between chocolate flavonoids and milk proteins. However, not all studies showed the negative impact of milk addition to food on polyphenol absorption. Keogh et al. [48] monitored the concentration of catechin and epicatechin in the blood after consumption of chocolate polyphenols with and without milk proteins. Results showed that milk protein did not influence the average plasma polyphenol concentration after ingestion. Contradictory results of these and many other studies were explained by the influence of polyphenol concentration. Milk could inhibit absorption in the case of lower polyphenol concentration, while it could have only minimal impact if the concentration is high [35]. In addition to food proteins, polyphenols can also bind to digestive enzymes and act as effective inhibitors as previously described in Chapter 3.

Only a few studies have investigated the interactions between polyphenols and dietary lipids. Since most polyphenols are water soluble, dietary lipids are considered to have a limited influence. Some studies, however, have observed a positive relationship. Ortega et al. [49] found that higher fat content has a positive effect on the stability of cocoa polyphenols in an *in vitro* digestion model.

Interactions between polyphenols and dietary fibers are important since these interactions have a significant role in the human body. Most non-extractable polyphenols with higher molecular weight (such as tannins and proanthocyanidins) are usually attached with covalent bounds to dietary fibers [28]. The bioavailability of polyphenols depends on the release of polyphenols from such a complex, which, in turn, depends on the polyphenols' structure, the complexity of the polyphenol-carbohydrate structure, and the possibility of enzymes to reach the carbohydrates [35]. According to Ortega et al. [50], soluble dietary fibers, in the *in vitro* digestion model, enhanced the stability of phenolic compounds during duodenal digestion. Since dietary fibers act as an entrapping matrix and restrict the diffusion of the enzymes to their substrates in the stomach and small intestine, many polyphenols reach the large intestine [51]. Regardless of their bioavailability, polyphenols, as strong antioxidants, may contribute to a healthy antioxidant environment, thus protecting the colonic lumen from oxidative stress, and, furthermore, polyphenols and carbohydrates that have reached the large intestine can have a beneficial effect on colon microflora growth.

6. Polyphenols as functional food components

Today's consumers' expectations of food, besides appropriate taste, appearance, and price, are more focused on positive health effects. Since consumers' awareness of health benefits associated with the consumption of food rich in polyphenols and preferences of herbal over synthetic products are increasing, meeting the consumers' expectations is a key to success.

The global polyphenol market was valued USD 757 million in 2015, and it is estimated to exceed USD 1 billion by 2022 [52]. The most successful applications of plant extracts containing polyphenols are fortification of beverages, while the most popular plant extracts used in beverages and other types of functional food are grape seed, green tea, and apple extract. The market for functional food and the number of studies focused on functional food with a positive effect on health beyond basic nutrition are constantly growing. The bioavailability of functional food components and the levels required in humans are critical factors necessary to optimize health benefits [53]. Polyphenols are the most numerous and widely distributed group of functional molecules. Studies have shown that products enriched with polyphenols could be useful for the dietary management of diabetes and cardiovascular disease prevention. Blueberry polyphenol-enriched defatted soybean flour was incorporated into a very high-fat diet of obese and hyperglycemic mice for 13 weeks. Compared with the control group (very high-fat diet containing defatted soybean flour), the diet supplemented with blueberry polyphenols reduced weight gain, improved glucose tolerance, and lowered fasting blood glucose levels and serum cholesterol [54]. The aim of an intervention study conducted by Sarriá et al. [55] was to evaluate the effect of two cocoa

functional products (one rich in dietary fibers and the other rich in polyphenols) on the markers of cardiovascular health. The most significant finding observed after consumption of both products was an increase in HDL cholesterol which was attributed to flavanols, the most common flavonoids in cocoa, while the fiber-rich product was associated with the hypoglycemic and anti-inflammatory effect. As recently reviewed by Tomé-Carneiro and Visioli [56], polyphenol-based nutraceuticals and functional food might be used as adjunct therapy for cardiovascular disease.

Since it is generally accepted that the bioavailability of polyphenols is rather low, recent scientific studies are focused on the enhancement of polyphenol bioaccessibility and the bioavailability rate in the body using encapsulation techniques such as spray-drying, freeze-drying, emulsions, and liposomes. Encapsulated polyphenols are more stable and are protected from light, oxygen, temperature, and moisture. Spray-drying is the most commonly applied encapsulation method in the food industry, transforming liquids into stable and easily applied powders, and can help in the controlled release of phenolic functional ingredients in the human body for more efficient nutraceutical usage [57]. Idham et al. [58] studied the degradation kinetics and color stability of spray-dried encapsulated anthocyanins with four different encapsulation agents (maltodextrin, gum Arabic, a combination of maltodextrin and gum Arabic, and soluble starch). Results have shown that the combination of maltodextrin and gum Arabic resulted in the highest encapsulation efficiencies as well as the longest shelf life and the smallest change in pigment color.

Emulsions are considered one of the most promising techniques for the protection and delivery of polyphenols, due to high-efficiency encapsulation, maintenance of chemical stability, and controlled release [59]. An emulsion is a mixture of two immiscible liquids, usually oil and water, with one of the liquids (the dispersed phase) being dispersed as small droplets in the other liquid (the continuous phase). Ru et al. [60] have shown that epigallocatechin-3-gallate (EGCG), the most abundant polyphenol in green tea, encapsulated in oil-in-water (O/W) emulsions demonstrated an improved anticancer effect, compared with free EGCG, on human hepatocellular carcinoma cell lines. The unpleasant bitter taste of flavanol monomers (catechin and epicatechin) could be successfully masked by using encapsulation, thus increasing flavanol delivery in the gut [61].

7. Conclusion

Polyphenols comprise a large group of phytochemicals with very diverse chemical structures and are considered as being the most common antioxidants in the diet. Since many foods and beverages contain a diversity of polyphenols, it is difficult to determine which specific compounds are directly responsible for beneficial health effects *in vivo*. The health effects of polyphenols depend on both dietary intake and bioavailability, which can vary greatly. The strongest evidence for the beneficial effects of polyphenols with regard to chronic disease, cardiovascular diseases in particular, exists for flavanol-rich foods. Most dietary polyphenols have relatively short half-lives once ingested, due to rapid metabolism, so it is important that their consumption is maintained throughout the life span. More detailed knowledge on the

relationship between the food matrix, processing, and bioavailability of polyphenols should lead to a better understanding of their role in human health and to the development of novel functional foods.

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