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Dietary Polyphenols and Their Perceived Health Benefits

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Abstract

This paper will consist of a compilation of information on polyphenol classes, dietary sources, and potential health benefits. Polyphenols can be classified as flavonoids, phenolic acids, lignans, or stilbenes. These molecules consist of over 500 plant metabolites that come from numerous food sources including various fruits, vegetables, grains, and beverages such as coffee, tea, and wine. The quantity of polyphenols in food vary greatly, as does their bioavailability for use in the body after consumption. Due to antioxidant and anti-inflammatory properties, polyphenols are being studied for effects on reducing the risk of cardiovascular disease. This paper will focus on structural differences of polyphenols, dietary sources of each class, and some general health benefits supported by current research.

1. Introduction

Polyphenols are a broad group of plant metabolites consisting of over 500 different molecules. These molecules can be broken down into different classifications based on their structure including flavonoids, phenolic acids, lignans, and stilbenes, some of which have subclasses as well. The differences in structure between the classes and subclasses are identified in this paper.

The range of foods that polyphenols can be found in is quite extensive due, in part, to the large number of molecules being represented. Because polyphenols are plant metabolites, they are only found in plant foods and their derivatives. Polyphenols are responsible for a large portion of taste and color in plant foods, as well as being protective agents for the plants themselves. The amounts found in foods vary greatly across the different classes. The bioavailability of these molecules also varies but does not necessarily align with the abundance of polyphenols in food. Bioavailability varies based on efficiency of absorption and rate of excretion.

Polyphenols are frequently studied because of their perceived health benefits when consumed. Eating a diet rich in polyphenols, like the Mediterranean diet, has been associated with antioxidant and anti-inflammatory affects. More recently, studies have looked at the effects of a polyphenol rich diet on cardiovascular disease risk factors.

2. Polyphenols – what are they?

Broadly, polyphenols are a group of molecules which are made up of multiple phenol groups. Phenols are derived from a phenyl group, also known as a benzene or aromatic ring, and a hydroxyl group (-OH). While this definition is adequate for application in organic chemistry, other characteristics need to be considered for further applications. A more comprehensive definition is compiled from the works of many scientists known as the White – Bate-Smith –

Swain – Haslam (WBSSH) definition. The WBSSH definition includes the following characteristics common to all polyphenols: (1) water-soluble, (2) molecular mass 500 – 4000 Da, (3) 12 – 15 phenolic hydroxyl groups, and (4) 5 – 7 aromatic rings per 1000 Da (Quideau, Deffieux, Douat-Casassus, & Pouységu, 2011).

In a biological sense, polyphenols are plant secondary metabolites which arise from phenylalanine or shikimic acid (Pandey & Rizvi, 2009). The molecules are involved in protecting the plant against pathogens, herbivores, radiation, extreme temperature, and drought, as well as aiding in growth and reproduction (Goszcz, Duthie, Stewart, Leslie, & Megson, 2017). When found in foods, polyphenols can add flavor, color, odor, or other effects like astringency to alter the mouthfeel of a food (Pandey & Rizvi, 2009).

Polyphenols are antioxidants in the most general sense. They are differentiated from other antioxidants due to their great variety of structures. Every polyphenol contains a base of phenolic hydroxyl groups with differences found in the functional groups and oxidation status which define their classification. Due to the complexity of biochemistry within cells, the definitive classification of some polyphenols is not possible as they contain multiple features from different categories. For this paper, the chemical classifications will be considered rigid and no molecules exist in more than one class.

Polyphenols consist of 4 classes, some of which are broken down into many subclasses, which can be seen in Figure 1. The four main classes include flavonoids, phenolic acids, lignans, and stilbenes. Phenolic acids have two subclasses: hydroxycinnamic acids and hydroxybenzoic acids. Flavonoids have six subclasses: flavonols, flavanones, flavanols, flavones, anthocyanins, and isoflavones (Tangney & Rasmussen, 2013). Flavonoids and phenolic acids are the most abundant classes of polyphenols with lignans and stilbenes being far less common (Scalbert & Williamson, 2000).

2.1. Flavonoids

Flavonoids are the most common polyphenol found in foods. Flavonoids start with a base structure of 15 carbons forming two benzene rings connected by three carbon atoms as part of a heterocyclic ring (C6-C3-C6) (Pandey & Rizvi, 2009). The heterocyclic ring contains one oxygen atom as well. As previously mentioned, flavonoids can be divided up into six subclasses including flavonols, flavanones, flavanols, flavones, anthocyanins, and isoflavones. The categorization of subclass depends on various derivations of this base structure. Molecules within each subclass differ by the quantity and position of hydroxylation.

The most basic flavonoid structure is the flavone structure which is comprised of the base structure and a ketone functional group on the 4th carbon of the heterocyclic ring. The flavone structure can then be built upon or changed to form the structure of isoflavones, flavonols, and flavanones. Isoflavones differ in that the 2-phenyl group becomes a 3-phenyl group. Flavonols contain the flavone structure with an additional hydroxyl group on the 3rd carbon spot of the heterocyclic ring next to the ketone functional group. Flavanones have the same structure as flavones, but do not contain a double bond between carbons 2 and 3 of the heterocyclic ring.

A flavanol has the general flavonoid structure (C6-C3-C6). Flavanols do not have a ketone functional group, but instead have a hydroxyl group on the third or fourth carbon. Anthocyanins start from the base flavonoid structure (C6-C3-C6) and contain an oxonium ion in the first position of the heterocyclic ring. An oxonium ion is a positively charged oxygen with three bonds.

2.2. Phenolic Acids

Phenolic acids are the next most abundant polyphenol found in foods. The base structure for phenolic acids is a single benzene ring, or phenol group, with carboxylic acid group attached, hence the name phenolic acid. Phenolic acids have two subclasses: hydroxycinnamic acids and hydroxybenzoic acids. Hydroxybenzoic acids have the carboxylic acid group attached to the benzene ring, and the hydroxycinnamic acids generally have three carbons between the benzene ring and the carboxylic acid group. Variations on these base structures create different molecules for the phenolic acids class.

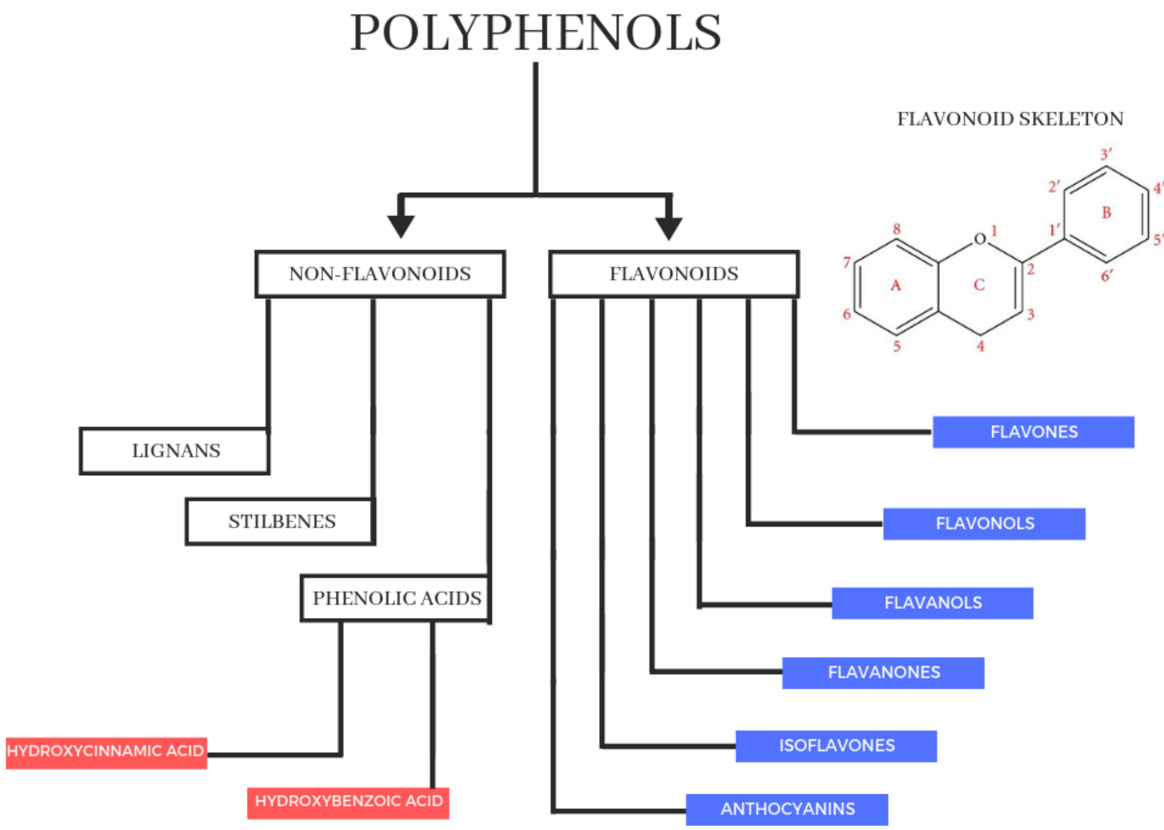
2.3. Lignans

Lignans are less common in foods than flavonoids and phenolic acids. The lignan base structure is made up of two phenylpropane groups linked together. Hydroxylation and the addition of functional group side chains create variations on this base structure to make up the lignan class.

2.4. Stilbenes

Similar to lignans, stilbenes are found in less frequently than flavonoids and phenolic acids in foods. The base structure for stilbenes consists of two benzene rings on either side of an ethylene group, or a carbon to carbon double bond (Chong, Poutaraud, & Hugueney, 2009). Stilbenes can be either *trans* isomers, with the rings on the same axial side of the double bond, or *cis* isomers, on the opposite axial side of the double bond. These conformations of the structure change the bend of the carbon chain, resulting in different reactivities and chemical properties. Further variations of the base structure, such as various levels of hydroxylation and side chains, create different molecules.

Figure 1: Polyphenol classifications



3. Foods high in polyphenols

Polyphenols are not distributed evenly throughout all levels of plant tissue. Likewise, the distribution of polyphenol classes among plants has no pattern. Some polyphenols may be found in all plants while others are specific to certain species. In addition to the variability of polyphenol content in plants, environmental factors and ripeness can also affect the amount of polyphenols found in plants (Pandey & Rizvi, 2009). In general, plants contain an assortment of polyphenols that vary between species.

Environmental factors have some effect on the polyphenol content of plants, but ripeness, storage, and cooking play bigger roles. As ripening occurs, phenolic acid content tends to decrease. Dry, room temperature storage can cause the loss of polyphenols whereas cold storage has less of an effect. The effect of cooking on concentration of polyphenols depends on the type of food as well as the type of cooking. For tomatoes and onions, boiling has the largest effect on polyphenol concentration decreasing it by about 80%, followed by cooking in a microwave oven at 65% and then frying at 30% (Pandey & Rizvi, 2009).

As previously mentioned, plants can contain a variety of polyphenols, but each class of polyphenols have various groups of plant foods they can be found in. Polyphenols are found in fruits, vegetables, as well as plant-derived foods and beverages (e.g., coffee, tea, juice, tofu, cereal). The more common polyphenols, flavonoids and phenolic acids, can be found in numerous food sources. In contrast, the less common polyphenols, lignans and stilbenes, are only found in a select few types of food sources.

Dietary availability of flavonoids and phenolic acids can be divided into food sources high in each specific subclass. With the flavonoid family having the most subclasses, these polyphenols cover a wide range of foodstuffs. Table 1 classifies example foods based on major polyphenolic constituents. The classes recognized by most scientific literature are organized in Figure 1 for easy reference.

Of the flavonoid subclasses, flavonols are the most common found in foods. Flavonols can be found in onions, kale, leeks, broccoli, blueberries, tomatoes, red wine, and tea. Flavonols are generally found in lower concentrations relative to other flavonoid classes in foods, at 15-30 mg/kg. Greater exposure to sunlight can dramatically affect the flavonol concentration due to their biosynthesis being stimulated by light (Manach, Scalbert, Morand, Rémésy, & Jiménez, 2004).

Flavones are found in a lower variety of foods compared to flavonols. Significant edible sources of flavones include parsley and celery, but flavones can also be found in the skin of citrus fruits, which humans generally do not consume.

Flavanones are most commonly found in citrus fruit like grapefruit, oranges, and lemons. The bitter flavor in some of these fruits comes from the flavanone content. Orange juice can contain 200-700 mg/L of flavanones, but the solid fruit and membrane surrounding the fruit have a much higher flavanone content. Oranges can contain 5 times the amount of polyphenols than orange juice (Manach et al., 2004).

Isoflavones are mostly found in soy and its derivatives. The amount of isoflavones found in soy and soy products varies based on growing conditions and processing. Isoflavone content in soybeans can vary from 580-3800 mg/kg of weight, and isoflavone content in soymilk can vary from 30-175 mg/L (Manach et al., 2004).

Flavanols are found in many fruits, with apricots containing the highest amount. Flavanols are also found in tea, chocolate, and grapes, and therefore wine. Tea is the richest source of flavanols with green tea containing up to 340 mg/L. Black tea contains about half the amount of polyphenols as green tea due to losing some to oxidation during fermentation (Scalbert & Williamson, 2000)

Anthocyanidins are responsible for the red, pink, blue, or purple pigment in fruits. They can be found in strawberries, cherries, raspberries, plums, blackberries, grapes, and currants as well as various vegetables and cereals. Subsequently, anthocyanidins can also be found in red wine. Quantities vary from 0.15 μg/kg to 4.5 μg/kg for the fresh fruits and 26 mg/L for red wine. The content of anthocyanidins found in food is generally proportional to the intensity of their color (Manach et al., 2004).

Hydroxybenzoic acids are found in small amounts in some red fruits, radishes, and onions. The highest source of this phenolic acid is found in tea. While the hydroxybenzoic acid content in these foods can be anywhere from 20 mg/kg to a couple hundred mg/kg of weight, tea can contain as much as 4.5 g/kg of weight (Manach et al., 2004).

Hydroxycinnamic acids are much more common in foods than hydroxybenzoic acids. These acids are commonly found in various fruits, coffee, and grains. One acid in particular, caffeic acid, usually makes up 75% to 100% of the hydroxycinnamic acids found in fruits. Caffeic acid is also considered to be the most common phenolic acid between both subclasses. Another significant hydroxycinnamic acid to note is ferulic acid. Ferulic acid makes up about 90% of total polyphenols found in wheat, about 0.8-2 g/kg (Manach et al., 2004).

Lignans can be found in very small amounts in grains, vegetables, and fruits. However, the main food source of lignans is seeds like flax seeds and sesame seeds. The quantities found in trace amounts in other foods do not compare to the concentration of lignans in flax seeds. Flax seeds can contain up to 3.7 g/kg of lignans which is about 1000 times greater than other food sources (Manach et al., 2004).

Stilbenes are found in trace amounts in foods. The only notable source of stilbenes is red wine. The amount found in wine varies from 0.3-15 mg/L, but is usually a small enough amount such that any beneficial effects of polyphenols are likely not because of stilbene contents. (Scalbert & Williamson, 2000)

Table 1: Examples of polyphenol food sources

Polyphenol Class	**Subclass**	**Food Source**	**Average Amount**
Flavonoids			
	Flavonols	Onions	0.3 µg/kg
		Tea	10-25 mg/L
	Flavanols	Green Tea	200-340 mg/L
		Black Tea	100-170 mg/L
		Red Wine	270 mg/L
		Apricots	250 mg/kg
	Flavones	Parsley	240-1850 mg/kg
		Celery	20-140 mg/kg
		Red Pepper	5-10 mg/kg
	Flavanones	Oranges	125-250 mg/L
	Isoflavones	Soybeans	580-3800 mg/kg
		Soymilk	30-175 mg/L
	Anthocyanidins	Strawberries	0.15 µg/kg
		Cherries	4.5 µg/kg
		Red Wine	200-350 mg/L
Phenolic Acids			
	Hydroxybenzoic acid	Tea	4.5 g/kg
		Flaxseed	6.7 µg/kg
	Hydroxycinnamic acid	Coffee	250-750 mg/L
		Wheat	0.8-2 g/kg
Lignans		Flax seed	8.7 µg/kg
		Sesame oil	15.9 µg/kg
Stilbenes		Red Wine	0.3-2 mg/L

4. Polyphenols in humans

4.1. Digestion and Absorption of Polyphenols

Much research that has been done regarding the polyphenol content in foods and an entire database exists with these amounts. The Phenol-Explorer database contains information on the polyphenol content of 452 different foods (Pérez-Jiménez, Neveu, Vos, & Scalbert, 2010). However, this data is not useful without some information on how polyphenols are digested and absorbed in the body, as well as how available they are for the body to use.

Polyphenols are generally not found isolated, and instead are usually bound to sugars or sugar alcohols called glycosides. The isolated polyphenols that are not bound to glycosides are called aglycones. Aglycones can be absorbed easily in the small intestine, while those bound to glycosides need to be hydrolyzed first before they can be absorbed. The only polyphenols absorbed in the stomach are anthocyanin glycosides, and the rest continue to the small and large intestines before absorptions (Goszcz et al., 2017).

Enzymes in the small intestine's brush border membrane hydrolyze corresponding sugars and release aglycones. The aglycones can then diffuse through the epithelial cell membranes without the sugars attached (Goszcz et al., 2017). The glycosides not hydrolyzed in the small intestine, as well as some more complex polyphenols, then reach the large intestine. The polyphenols that make it past the small intestine are hydrolyzed by the microflora of the large intestine. Because the surface area of the large intestine is much less than the small intestine, aglycones are not absorbed as readily in the colon. Therefore, polyphenols hydrolyzed in the colon are not as efficiently absorbed (Manach et al., 2004).

The difference in absorption of various polyphenols is demonstrated in the amount of intact polyphenols that are excreted in the urine. Anthocyanins, which are absorbed first in the stomach, generally have the lowest percent recovery in urine (as low as 0.01%), while some flavonoids that cannot be absorbed until they reach the large intestine can have a much larger percent recovery in urine (as high as 43%) (Zamora-Ros, Touillaud, Rothwell, Romieu, & Scalbert, 2014). However, along with intact polyphenols, all forms of metabolized polyphenols are excreted from the body within 2 to 4 hours after ingestion (Goszcz et al., 2017).

As just discussed, the structure of polyphenols greatly affect the rate and efficiency of their absorption into the body, but other factors can also affect the bioavailability of these molecules. Interaction between other compounds, like protein, carbohydrates, and fat, can also play a role in polyphenol absorption (Goszcz et al., 2017). Polyphenols can enhance the expression of some protective proteins which can reduce the bioavailability by degrading or inactivating the molecules (Yamagata, Tagami, & Yamori, 2015).

Bioavailability is important because the polyphenols that are most commonly consumed in our diets are not necessarily the most bioavailable due to inefficient absorption or rapid excretion (Manach et al., 2004). Quercetin, for example, is a common flavonol found in tea, wine, and many fruits and vegetables, but it is rapidly excreted and can only be absorbed as an aglycone (Scalbert & Williamson, 2000). Polyphenols are greatly modified between how they are found in food to their form that arrives at blood and tissues. Polyphenols are conjugated in the endothelial cells of the small intestine as well as in the liver. Conjugation of polyphenols is done via sulfation, methylation, or glucuronidation, the addition of glucuronic acid (Pandey & Rizvi, 2009).

4.2. Potential Health Benefits

Many studies have been done examining the effects of a polyphenol rich diet on the body and some potential health benefits that may occur (Guo et al., 2016; Medina-Remón et al., 2015). Polyphenols have antioxidant properties due to their hydroxy groups that are able to pick up free oxygen and nitrogen molecules that are otherwise pro-inflammatory (Tangney & Rasmussen, 2013). The antioxidant activity of a polyphenol varies based on its structure. The efficiency of antioxidants is based on if the molecule has one or more of the following structural features: an o-diphenolic group, a 2-3 double bond, and hydroxyl groups at the third and fifth carbon (Bravo, 1998). In the past, studies only looked at the antioxidant properties of polyphenols, but the focus now is in lowering the risk for developing cardiovascular disease (CVD).

There are many unalterable risk factors for CVD like genetics, age, and sex, so changing the controllable risk factors for CVD greatly decreases the chance for development. These controllable risk factors include smoking, high low-density lipoprotein (LDL) and low high-density lipoprotein (HDL) cholesterol, hypertension, sedentary lifestyle, obesity, and type 2 diabetes. Several recent studies have shown an association between consuming a polyphenol rich diet and lowering some CVD risk factors, specifically hypertension, cholesterol, and plasma glucose levels (Guo et al., 2016; Medina-Remón et al., 2015; Noad et al., 2016; Vetrani et al., 2018; Vitale et al., 2017).

Some recent studies on lowering CVD risk factors with polyphenols utilize their antioxidant activity as part of the study results. Medina-Remón et al. measured total nitric oxide in plasma samples as a way to observe polyphenol antioxidant activity in the blood as a measure of lowering blood pressure. Many studies take urine samples to measure isoprostanes excreted in the urine. Isoprostanes are a marker for oxidative stress, so when isoprostane levels in the urine decrease after being on a polyphenol rich diet, oxidative stress decreases as does blood pressure (Vetrani et al., 2018). Because hypertension is one of the controllable risk factors for CVD, lowering blood pressure via the antioxidant activity of polyphenols is important to understanding the health benefits polyphenols can have.

5. Conclusion

This paper attempted to compile information on polyphenols classes, dietary sources, and potential health benefits. Polyphenols can be divided into classes based on their structure. Classes include flavonoids, phenolic acids, lignans, and stilbenes. The amounts found in plant foods and their bioavailability vary with the complexity of the molecules' structures. Antioxidant and anti-inflammatory qualities mean that polyphenols are being studied for effects on lowering risk factors of diseases such as those for CVD. Due to the large extent of polyphenol molecules found in foods, more research still needs to be done on the effects of specific classes as opposed to polyphenols as a whole.

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