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Benefits and Preparation Effects on Polyphenol-Rich Fruits and Vegetables Towards Cardiovascular Disease Prevention

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Abstract

Individuals with cardiovascular disease are advised to consume fruits and vegetables due to their potential health benefits of their polyphenol-rich components. The main precursors that lead to cardiovascular disease are endothelial dysfunction and arterial stiffness. These metabolic dysfunctions can be improved by bioavailability of polyphenol-rich foods such as hesperidin from citrus fruits or anthocyanidins that give the color of fruits and vegetables. Polyphenol-rich foods can increase beneficial biological processes including the expression of nitric oxide in the blood vessel to enhance vascular tone by vasodilation. However, polyphenols can be lost during absorption and post-absorption by interactions with other macromolecules. Additionally, the cooking methods and preparation of certain polyphenol-rich fruits and vegetables can cause extreme loss of polyphenols. Recent studies have demonstrated various cooking methods that can enhance the nutrient quality of polyphenols and their bioavailability. Understanding the absorption, biological processes and cooking methods of polyphenol-rich fruits and vegetables can help link the benefits of prevention or treatment in cardiovascular disease risk factors.

Keywords: Polyphenols; Phenolic acid; Cardiovascular disease; Nitric oxide; Endothelial function; Arterial stiffness

Introduction

Cardiovascular disease (CVD) has the highest mortality rate worldwide. According to the American Heart Association [1], the leading cause of death in the United States is Coronary heart disease (43%) followed by stroke (16.8%), heart failure (9%), high blood pressure (9.4%) and of diseases in the arteries (3.1%). Health professionals usually recommend a high fiber diet which includes fruits and vegetables to decrease the risk of chronic disease, including CVD [1]. These fruits and vegetables have high-quality phytonutrients especially a polyphenol-rich component that has been studied tremendously towards its benefits for CVD. The absorption of polyphenols is a fundamental concern due to its bioavailability and bioaccessibility that can help prevent some biological processes involved in the development of CVD [2]. Bioaccessibility is termed as the amount of an ingested nutrient that is available for absorption after digestion. The concept of bioavailability is defined as the proportion of an antioxidant that is digested, absorbed, and utilized in metabolism relying on the amount of antioxidants absorbed. Usually, polyphenol-rich fruits and vegetables are consumed with different macromolecules such as carbohydrates, lipids, and proteins, which can have chemical interactions interfering with the bioavailability of polyphenols [3]. In addition, the preparation of certain fruits and vegetables can reduce their polyphenol bioavailability and bioaccessibility which decreases the beneficial factors towards CVD. The main two CVD risk factors are endothelial dysfunction and arterial stiffness but increased absorption of polyphenols can better regulate endothelial function and vasodilation [2]. The purpose of this review is to understand polyphenol-rich fruits and vegetable absorption, endothelial benefits, and different cooking preparation that can either enhance or lessen their interactions with molecular biomarkers that can treat or prevent CVD risk factors.

Literature Review

What are polyphenols?

In the 1930s, one of the polyphenols called hesperidin was expected to be classified as a vitamin P but later discovered a protective factor on the vascular system during the 1950s. Around the years of the 1990s, polyphenols were used as a patent medicine to cure any type of diseases or illness because it was characterized as antioxidants [4]. Eventually, polyphenols drew attention on the French paradox because of their low incidence of CVD risk in the French population despite the high-fat content in their diet [5]. Ultimately, polyphenols have been revealed to be associated with many biological effects on biochemical interactions in several pathways depending on their bioavailability. Polyphenols are a diverse group of molecules that originate from plant-based foods and have been termed as non-nutrients, plant secondary metabolites, phytonutrients, antioxidants, dietary bioactive and protective factors. Additionally, the phytochemicals do not have a specific chemical term and can be referred to as flavonoids or polyphenols. For the purpose of this review, polyphenols will be used instead of flavonoids from here on. There is an abundance of chemical types but the number of polyphenols that are important in the diet is relatively small. The main polyphenols that are mostly examined based on our diets are demonstrated on Table 1 by their classes and subgroups [4]. Most of the common classes of polyphenols and their biochemical pathways related to bioavailability are adequately absorbed and well understood.

Absorption of polyphenols

In general, polyphenols are bound to a sugar molecule, glycoside, and are cleaved for increased absorption in the lumen of the small intestine [5]. Then, glycoside is removed from the polyphenol skeleton and passes through the gastrointestinal wall into the bloodstream by

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Classes	Subgroups
Flavanols	Catechins and Tannins from Tea and Cocoa
Flavanones	Hesperidin, Naringenin from Citrus Fruits
Flavonols	Quercetin, Epicatechin from Tea, Apples, Broccoli and Onions
Hydroxycinnamic acids	Chlorogenic Acids (Phenolic acid) from Coffee, Fruits, and Vegetables
Anthocyanidins	Anthocyanins and Proanthocyanidins are Colored Polyphenols in Fruit and Vegetables; Mainly found in Berries, Grapes, and Cocoa.

Table 1: Classes and subgroups of the main polyphenols consumed [4].

enzymatic actions [6]. During post-absorption, the polyphenol gets taken up by the liver and other organs producing secondary metabolites that utilizes their beneficial biological effects [2]. The unabsorbed portion of polyphenols passes through the colonic micro flora and convert to simple phenolic acids. This explains that polyphenols can either be absorbed into the bloodstream or utilize its antioxidant activity in the bacterial environment of the large intestine [7]. Furthermore, the secondary metabolites formed by the small intestine, liver and colonic micro flora can increase antioxidants to prevent certain biological processes linked to CVD [2]. Polyphenol-rich fruits and vegetables are consumed with different macromolecules that can have chemical interactions interfering with the bioavailability of polyphenols [8]. For instance, dietary fiber can reduce the bioavailability of other macronutrients and some micronutrients including the absorption of polyphenol compounds such as carotenoids [8]. Dietary fiber reduces the rate of released nutrients because it prolongs gastric emptying. This can enhance absorption, trapping of antioxidants and increase the viscosity of gastric fluids. Resulting to this, there an increase of satiety due to the decrease of the peristalsis mixing process along with the enzymes to their substrates, bile salts to micelles and soluble antioxidants to the gastrointestinal wall. The micelle formation with carotenoids is interfered by dietary fiber that trap bile salt molecules and block the passive absorption in the small intestine [9]. Dietary fiber in the gastrointestinal tract can limit certain polyphenol absorptions even though polyphenol-rich fruits and vegetables are recommended for the prevention or treatment of CVD risk factors [2]. Still, more research is needed to explain certain interactions of macromolecules that can affect polyphenol absorption and their biological pathways.

Endothelial and arterial function

Polyphenol-rich foods such as cocoa improve endothelial function, reduces oxidation of low-density lipoprotein (LDL) and inhibit activation of platelet aggregation [4]. Recent studies have shown that a regular consumption of cocoa can reduce blood pressure and blood cholesterol [4,10]. The regulation of endothelial function is part of the molecular level interactions with nitric oxide (NO) metabolism in the blood vessel that induces vasodilation and lowering blood pressure [10]. One of the most active polyphenol-rich food is tea which is rich in the polyphenol catechins. Black tea has the most catechin that lowers the effect on blood pressure, LDL-cholesterol with no effects on high-density lipoprotein (HDL) [11]. Furthermore, quercetin is known to reduce platelet aggregation, thrombus formation, inflammation, and endothelial dysfunction. Polyphenol-rich foods high in quercetin are found in onions, tea, potatoes, apples, and broccoli. Additionally, hydroxycinnamic acids in coffee can increase glutathione levels which prevents oxidation and protect against DNA, lipid and protein damage [12].

A randomized controlled clinical study was done on flavonoid-rich Cripps Pink apple skins with individuals who are at risk for CVD to improve endothelial function [13]. Due to this randomized controlled clinical study, the term flavonoids are used instead of polyphenols and will be used only for this section of the review. According to the study, a higher apple intake has been associated with lower risk of abdominal aortic calcification, coronary heart disease and stroke. Additionally, most apple varieties are rich in quercetin, epicatechin and anthocyanins which are responsible for the red color of the concentrated skin. The study included 30 volunteers from Perth, Australia that either had elevated blood pressure, blood sugar concentrations, fasting cholesterol or central obesity. The participants needed to cut down on other flavonoid-rich foods such as tea, red wine, dark chocolate, and onions for two weeks before and throughout the duration of the study. The control group had a low-flavonoid apple (LFA) blended with water and skinless Cripps Pink apples. The treatment group had a high-flavonoid apple (HFA) with one whole Cripps Pink apple plus the skin only of a second Cripps Pink apple blended in water. The researchers discovered a high concentration of quercetin and epicatechin in the HFA group, high anthocyanins in both groups, and chlorogenic acid in the LFA group. To later asses endothelial function, the brachial artery diameter was calculated to determine flow-mediated dilatation (FMD). There was a significant improvement in FMD with HFA group (p-value of <0.001) after 2 hours of consumption [13]. This was due to the high metabolites of quercetin which has been proven to affect NO bioavailability and enhance vascular tone [11]. The health benefits of polyphenol-rich apples can have improvements in endothelial function reducing the risk of CVD based on its high quality of quercetin, epicatechin, and anthocyanins [13]. Anthocyanins and Proanthocyanidins have been widely studied on reducing endothelial inflammation by inhibiting harmful radicals and enhancing NO production [14]. Inflammation is caused by macrophages, growth factors, adhesion molecules, and cytokine expressions of tumor necrosis factor (TNF-α) and interleukins (IL-6) in the vascular endothelial cells [15]. Anthocyanidins reduces oxidative stress, protects the intestinal mucosa and enhances absorption due to the high glutathione scavenging for superoxide/hydroxyl radicals [14]. Proanthocyanidins in grape seed can stimulate NO production by protein kinase B activation (Akt kinase), improvements of cellular function and nitric oxide synthase (NOS) regulation [16]. This results in endothelium relaxation of blood vessels through the interactions of NOS [17]. Moreover, an endothelial plasma membrane carrier that transports flavonoids, bilitranslocase, is thought to be the trigger of anthocyanin-induced vasodilation [16]. Anthocyanidins can change inflammatory cytokines and limit adhesion molecules expressions by decreasing vascular endothelial growth factor (VEGF) during immune cell migration to an injured area [15]. Additionally, Anthocyanidins from consumption of red wine can have a cardiovascular protective effect by improving lipid homeostasis and inhibit LDL oxidation more than antioxidants like vitamin C/E [18]. Anthocyanidins are essentially found on the skin of fruits and vegetables but have crucial functions in suppressing CVD bioactive properties [14]. Hyperglycemia can lead to diabetes and eventually lean towards endothelial dysfunction causing CVD [19]. A polyphenol called caffeic acid, which are mainly found in coffee, has been associated with glucose metabolism and improving vascular function. Generally, caffeic acid is part of hydroxycinnamic acid, chlorogenic acid, ferulic acid and dihydroferulic acid metabolites. Glucose metabolism is regulated by the uptake of glucose into the cell by glucose transporter 4 (GLUT4) and factors such as a highcalorie diet can cause a decrease in GLUT4 expression. An *in-vitro* experiment was done on 6 plant derived dietary phenolic compounds (Chlorogenic acid, Ferulic Acid, Protocatechuic-Acid, Dihydroferulic Acid, Quercetin, Gallic Acid) to take note of other compounds that can increase glucose metabolism. These were studied on rat L6 skeletal muscles that naturally express GLUT4 and induce differentiation of myotubes, a developmental stage of muscle fibers. Overall, the dihydroferulic acid showed better effects on improving cellular uptake of GLUT4 regulating glucose metabolism and decrease CVD risk. However, more research is needed because the study experimented *in-vitro* and there is inadequate information in the actual *in-vivo* bioactivity of dihydroferulic acid [19]. Arterial stiffness is one of the precursors of CVD risk factors and is a reversible process by enhancing dietary changes especially in polyphenol-rich fruits and vegetables [20]. The prevalence of arterial stiffness can be due to vascular aging releasing vasoactive endothelial mediators causing deterioration in vessel elasticity. Usually, women have regulated estrogen production which is a protective factor against the development of CVD. However, women during the menopausal stage have suppressed production of estrogen inducing a greater risk of heart disease. A randomized controlled crossover clinical study was done on healthy postmenopausal women consuming grapefruit from a duration of 6 months on protective effects on arterial stiffness. Grapefruit is considered a citrus fruit that is high in hesperidin and naringenin that exert anti-inflammatory, anti-atherogenic properties, and improvements of vascular activity. The researchers of this study investigated whether grapefruit polyphenols could have protective effects on vascular function. The study was done in the Clermont-Ferrand region in France with 52 eligible participants who were nonsmoking Caucasian women aged between 50-65 years old. The participants had menopause between 3-10 years with a normal to overweight BMI, normal blood pressure, normal blood lipid levels, and electrocardiogram. They had to consume either 340 ml “control drink” or 340 ml of “grapefruit juice” both with the same macro/micro-nutrients and calories (110 kcal). Additionally, the control drink was prepared without naringenin and the grapefruit juice had 212.9 mg of naringenin. The participants were required to minimize their intake of citrus foods and consumption of polyphenol-rich beverages. The participants had to record their entire food intake on three consecutive days directly after consumption including the name of the food, preparation methods, recipes and portion sizes. A dietitian had to screen all the 3-day food questionnaires to clarify entries, probe forgotten foods and to check portion sizes. To measure arterial stiffness was by the pulse, which travels at a higher velocity in stiff arterial vessels, and calculated from pulse transit time and the distance traveled between the carotid artery and femoral artery. A noninvasive device was used for online pulse wave recordings and automatic distance/transit time calculations (PWV). After the 6-month intervention, the PWV between carotid and femoral arteries were significantly lower in the grapefruit juice consumption than the control drink consumption (p-value of 0.019). One of the weaknesses of this study was not identifying the biochemical changes in the reduction of arterial stiffness. The study demonstrated that increased naringenin consumption can lower arterial stiffness in healthy postmenopausal women [20].

A meta-analysis have been done on prospective cohort studies due to limited comprehensive investigation and assessed polyphenols intake and mortality from CVD [21]. The researchers have found that the development of CVD can be prevented by antioxidants, anti-inflammatory vasodilator functions. Additionally, polyphenols can reduce oxidative stress damage by free radicals scavenging activity via glutathione. Plus, polyphenols have antioxidant properties reducing LDL, which is considered the central cause of atherosclerosis, by inactivating reactive oxygen species. Polyphenols can influence FMD by improving levels of NO for vasodilation ameliorating endothelial function. Additionally, the antioxidant property of polyphenols are linked to anti-inflammatory actions that are more reliable than vitamin C and E. Furthermore, certain polyphenol components can reduce the risk of type 2 diabetes along with the progression of CVD. Lastly, polyphenols can alleviate the blood vessel endothelium by reducing the risk of clot formation due to their anti-aggregation properties [21].

Food preparation methods and their effect polyphenols

Food processing usually cause losses in polyphenol content by oxidation, enzymatic action, removal of skins or seeds, and leaching into oil or water that is then discarded [22]. The common cooking methods for legumes and vegetables are explained on Table 2 [23]. The factors that are part of domestic processing are washing, peeling, cutting, chopping, soaking, heating, and freezing can damage the cell structure of certain fruits and vegetables decreasing their polyphenol content. The most studied vegetables based on polyphenol content are broccoli, onions, potatoes, tomatoes, and legumes such as beans [22,23]. There are several ways to enhance the bioavailability of healthy nutrients through proper selection of cooking methods that can help treat or prevent the risk of CVD [23]. The changes caused by food preparation can affect the flavor, texture, appearance and the nutritional quality of foods. For instance, chopping vegetables can alter the bioactive compounds and bioavailability of polyphenols. Steaming is the best method to maintain the polyphenol content of broccoli but if prolonged can cause losses of quercetin [22]. Therefore, steaming broccoli should be 7.5 minutes to retain the nutritional quality including quercetin [23]. The overall losses of polyphenols from potato were relatively mild regardless of the type of cooking method. Also, boiling of whole potatoes for 60 minutes did not result in a reduction of folate or any polyphenol components [23]. In relation to cooking effects, there were different levels of polyphenol gains and losses due to the type of cooking method with onions [22,23]. There was an increase of polyphenol concentration when onions were sautéed and oven baked but decreased during boiling. Therefore, onions should be cooked less than 5 minutes to retain over 80% of their polyphenols.

Cooking Method	Description
Steaming	To cook food that is suspended, generally in a basket, over simmering liquid in a covered pot set on the stovetop.
Roasting	To cook foods in a pan in a hot oven.
Boiling	To cook foods in boiling liquid in a pot set on a hot burner.
Frying	To cook in a hot oil in a skillet on a hot burner.
Sautéing	To cook foods in a thin film of hot oil in a skillet set on a hot burner
Sous vide	To cook in a vacuumed plastic pouches at precisely controlled temperatures
Microwave	To cook by placing the food in the path of a microwave (induced molecular friction in water molecules will to produce heat).
Pressure-cooking	To cook food using water or other liquid in a seal pot in a pressure cooker or an autoclave.

Table 2: Different cooking methods [23].

Additionally, microwaving onions instead of using a pressure-cooker can minimize the losses of insoluble dietary fiber components that have protective factors towards CVD. Lastly, bile acid binding lowers the levels of cholesterol in the blood by certain cooking methods. For instance, steaming and sautéed beets, eggplants, asparagus, carrots, green beans, and cauliflower can improve bile acid binding and lower LDL cholesterol reducing the risk of atherosclerosis. Legumes are considered heart healthy and recommended due to its high fiber and mineral contents that can improve blood LDL cholesterol levels. Though the preparation of certain legumes can severely decrease their bioavailability of certain polyphenols. For instance, soaking beans before cooking them can enhance the polyphenols bioavailability and decrease cooking time. During the soaking method, the water diffuses into the starch granules and protein fraction facilitating gelatinization and protein denaturation that later softens the texture of the beans [22]. However, this can be improved by adding salt into the soaking water to eliminate tannin contents, a class of antioxidant polyphenols that can impair the digestion of various nutrients. Then, discarding the soaking solution and cooking with fresh water is the best way to improve the nutritional quality of the beans [23]. Overall, the knowledge of affected polyphenols based on various methods of cooking and preparation is essential to improve beneficial facilitation of protective factors to control CVD progression. Dietary fiber can lower polyphenol absorption but their bioavailability can be improved by the proper cooking method. Health professionals recommend fruits, vegetables and legumes but lack the explanation of the best type of cooking methods to prevent loss of certain polyphenols presented in foods. Understanding the different cooking techniques and preparations of certain fruits and vegetables is a necessity because of their different polyphenol content.

Discussion

The notion of bioavailability is closely correlated with the concentration of polyphenols at the target cell or tissue after absorption, metabolism, distribution, and excretion [24]. The absorbed polyphenol compounds are bioavailable and are able to pass through the small intestine due to hydrolyzation of glycosides [6]. The polyphenols that have low bioavailability and insufficient absorption due to dietary fiber in the small intestine can travel to the colon as phenolic acids. The benefit of traveling to the bacterial micro flora is that it provides a healthy antioxidant environment by scavenging free radicals even though the bioavailability is low [7]. This became a consequential issue on supplementation of polyphenols to promote bioavailability. In most cases, polyphenols act with other nutrients because it is already consumed with different foods [4]. Additionally, supplements may have modified bioavailability and individuals can replace fruits and vegetables with supplements leading to malnourishment. If supplementing polyphenols are taken without food, there would not be any effects on biological factors to improve risk factors of CVD [4]. There is still more research needed to completely understand the absorption of all classes of polyphenols to really recommend a supplementation.

A healthy endothelium is fundamental to cardiovascular health and endothelial dysfunction is a prominent precursor of CVD especially with stroke and atherosclerosis. The improvement in endothelial function with HFA in the previous study was due to high plasma quercetin, epicatechin and anthocyanins concentration of the Cripps Pink apple skin. Additionally, the researchers noticed circulating quercetin, epicatechin, and anthocyanins 3 hours after ingestion with the idea that they were absorbed in the small intestine. The polyphenols that benefited endothelial function was based on NO synthase activity enhancing the NO bioavailability to regulate vascular tone [13]. Anthocyanidins are known to have beneficial effects on various signaling pathways and mechanisms especially in NO production. As previously stated, anthocyanidins increase glutathione scavenging superoxide and hydroxyl radicals protecting the intestinal mucosa for enhanced nutrient absorption. This can be the reason that Cripps Pink apple skins had improvements in endothelial function from anthocyanidins being one of the highest polyphenol in plasma concentration. Another finding was based on consuming grapefruit juice that had naringenin resulting in lowering arterial stiffness in postmenopausal women. This study proposed that consuming citrus fruit juices high in hesperidin and naringenin could be a reliable mechanism to improve endothelial function. However, the study did not describe the main biological process that contributed to a decrease in arterial stiffness indicating that more experimentation is needed to understand the full mechanism of citrus fruit polyphenols with CVD [20]. As previously stated, coffee is associated with hydroxycinnamic acid metabolites which are a part of caffeic acid, chlorogenic acid, ferulic acid and dihydroferulic acid. The phenolic acid that may play a role in glucose homeostasis by improving uptake of GLUT4 transporters is dihydroferulic acid [19]. The research on dihydroferulic acid on T2D and CVD is very limited to really suggest positive results of consuming coffee to lower the risk of those chronic diseases. Though, the study was informative enough to suggest more experimental human studies on dihydroferulic acid to reduce risk of T2D and CVD. Ultimately, the absorption and benefits of polyphenols all come down to cooking methods and preparations of certain fruits and vegetables. Cooking methods are usually shown in dietary questionnaires and should be considered when estimating intake of polyphenols [24]. As stated before, foods must be considered independently when cooking for optimization of polyphenol content. Additionally, chemical structures greatly affect the degree of loss regarding individual polyphenols. This may partially explain variations between fruits and vegetables since they each carry a different profile of polyphenols [23]. It is known that nutrient losses occur during styles of cooking methods but learning how to prepare foods differently for the sake of polyphenol contents can accommodate individuals with CVD. Many randomized controlled clinical studies (RCT) support the protective effects of polyphenol-rich foods to prevent or treat CVD. However, the evaluation of polyphenol intake is still inclined to bias due to limitations of self-reported diet recalls and lack of biological process [16]. Polyphenol consumption assessed by food frequency questionnaires or diet histories are considered self-reported and can be a source of error. Plus, some of the RCT assessed to some degree the absorption and metabolism of polyphenols which is a significant factor in building potential cause-and-effect associations. Additionally, studying the effect of polyphenol-rich foods on CVD risk is biased without taking into account other non-polyphenol bioactive components such as carotenoid, lignin's, phytosterols, sugars, fiber, lipids, vitamins, and minerals [24]. Most of the studies solely used the terms micronutrients and macronutrients and not specified during the intervention [13,20,21,24]. The RCT on polyphenols need to account for important factors of absorption and certain bioactive processes that affected their results.

Conclusion

There are numerous studies of polyphenol-rich fruits and vegetables, absorption, endothelial function and cooking methods to prevent or treat CVD. The absorption of certain polyphenols is important to understand because of their specific bioactive components related to CVD processes. There are certain polyphenols that induce NO production to regulate vascular tone, increase vasodilation and lower blood pressure to improve endothelial function. Additionally, the cooking methods and preparation of certain polyphenol-rich fruits and vegetables is the first step to adjusting polyphenol bioavailability. For future improvements, health professionals should include brochures on different fruits and vegetables with their polyphenol contents and explanations on their beneficial factors. Moreover, the brochure should include different cooking methods to enhance the polyphenol bioaccessibility and bioavailability. There is enough research on the known dietary polyphenols that can be useful to improve CVD risk factors even though more studies are required to fully understand all functions of polyphenol classes.

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