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REVIEW

Benefits of Green Tea Polyphenols for Kidney Health: A Literature Review

Nadia Warda Sekar Sari, Trina Ekawati Tallei* and Beivy Jonathan Kolondam

Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Sam Ratulangi, Manado, North Sulawesi, 95115, Indonesia

* Correspondence: trina_tallei@unsrat.ac.id

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Abstract

The issue of kidney health has emerged as a global public health concern. Kidneys play a vital role in eliminating toxic substances and maintaining fluid and chemical balance in the body. Preserving kidney health is tantamount to safeguarding overall bodily health, as kidney damage can adversely affect other organs and organ systems. This can give rise to various ailments and compromise one's physical condition. Throughout ancient history, plants have been employed for medicinal purposes in treating a wide array of ailments with one such plant being tea (*Camellia sinensis* L). Tea is renowned for its antioxidant and anti-inflammatory properties. It contains bioactive compounds, notably polyphenols, which contribute to enhancing health. Polyphenols serve as therapeutic agents for the kidneys and can prevent the onset of other degenerative disease. Prior research has demonstrated that EGCG, a derivative of polyphenols, can safeguard the kidneys against ischemia-reperfusion injury, kidney fibrosis, and inflammation. Catechins, a subcategory of polyphenols, act as antioxidants, anti-inflammatories, and anti-apoptotic agents, thereby shielding kidney cells.

Introduction

Throughout history, our ancestors extensively utilized plants for the maintenance, prevention, and treatment of various ailments [1–3]. One such plant is tea (*Camellia sinensis* L.). Tea is derived from the leaves of the tea plant, a member of the Theaceae family. Presently, tea has gained worldwide recognition as one of the most popular beverages globally, ranking second only to water in consumption. Tea offers numerous health benefits, serving as an antioxidant, aiding in cellular regeneration, and reducing cholesterol levels in the bloodstream [4]. Tea is categorized into four main types: green tea, black tea, oolong tea, and white tea. The processing of tea involves several stages, including post-harvest drying, withering, rolling, wet sorting, and storage. Green tea is a non-fermented type, black tea undergoes prolonged fermentation, oolong tea experiences rapid fermentation, and white tea is considered a semi-fermented tea [5]. Tea originates from the leaves of the *Camellia sinensis* L. plant, which initially grew in China and later spread to India, Sri Lanka, and other countries. Currently, tea plants are cultivated in approximately 30 countries located in regions with tropical and subtropical climates, characterized by adequate rainfall, good drainage, and slightly acidic soil [6]. The primary component in fresh tea is polyphenols, which constitute 30% of the dry weight of young tea leaves. These four tea types exhibit significant differences in their polyphenol content, despite originating from the same plant [7]. Polyphenolic compounds, particularly flavonoids, have known health benefits and represent the largest class of compounds within this category [8].

The flavonoid compounds with high antioxidant activity are found in catechins. Catechins consist of epigallocatechin gallate, epigallocatechin, epicatechin gallate, and epicatechin [7]. Polyphenols are the dominant compound group in tea and serve as a nutritional source that enhances the antioxidant system to counteract reactive oxygen species (ROS). Antioxidants are

compounds capable of inhibiting, preventing, and repairing damage caused by oxidation processes and oxidative stress. ROS can damage cell membranes, nucleic acids, proteins, and lipids [9]. Free radicals can induce oxidative stress characterized by cell membrane and protein damage, including enzymes, due to disruptions in membrane permeability and membrane function itself [10]. Scientific evidence indicates that ROS and inflammation play a significant role in the pathophysiological processes of kidney diseases. The kidneys are sensitive to ROS attacks, and oxidative damage is often associated with various renal disorders, including acute kidney failure [11]. In humans, almost all end products of metabolism are excreted through the liver and kidneys, and when organs such as the liver or kidneys are compromised, their ability to handle metabolic products or waste can be affected [12]. One of the primary functions of the liver is to modify, eliminate, and metabolize substances in the body, while the kidneys are responsible for blood filtration and waste removal in the form of urine. Disorders in these organs can result in the accumulation of metabolic products or waste that should be excreted [13].

Several studies have indicated that green tea may provide significant health benefits. Polyphenols contribute to enhancing health and serve as therapeutic agents for kidney diseases, preventing the onset of degenerative diseases such as cancer, cardiovascular diseases, neurodegenerative disorders, and metabolic disturbances [14]. In addition to polyphenols, tea also contains various chemical elements such as tannins, alkaloids like caffeine and theobromine, polysaccharides like D-rhamnose, L-arabinose, and minerals like sodium, magnesium, potassium, phosphorus, titanium, zinc, and iron [7]. Green tea is widely consumed as a dietary supplement. In countries like China and India, green tea is used to control bleeding, heal wounds, and improve heart health. Polyphenols are abundant in our daily diet and represent the most plentiful source of antioxidant intake [15].

Polyphenols have the potential to act as therapeutic agents against kidney diseases. The effects of ROS species and inflammation play a crucial role in the pathophysiology of kidney diseases [11]. However, research on the effectiveness of polyphenols in kidney therapy remains limited, necessitating more comprehensive studies. The objective of this review is to analyze the effects of polyphenolic compounds from green tea in promoting kidney health by considering their antioxidant and anti-inflammatory benefits. This review article constitutes a descriptive study with the aim of examining the benefits of tea polyphenols for kidney health by synthesizing findings from various scientific literature sources.

Methodology

The methodology used to write this review article was based on the exploration of literature in both Indonesian and English languages through platforms such as Google, PubMed, Science Citation Index, Scopus, and others. The selection of relevant literature concerning the benefits of tea polyphenols on kidney health involved the use of keywords such as "tea plant," "compounds in tea," "benefits of tea polyphenols," "kidney health," and "reactive oxygen species" during the literature search. The article provided an overview of the role of polyphenols in safeguarding the kidneys within the human body.

Types of Tea Polyphenols

Phenolic compounds are chemical compounds that attach to an aromatic ring with one or more hydroxyl groups. Compounds with multiple phenolic groups are referred to as polyphenols. Polyphenols belong to the class of phytochemicals commonly found in plants. These polyphenolic compounds are most abundant in green tea leaves. Polyphenols can be further categorized into three subclasses, namely phenolic acids, flavonoids, and non-flavonoids. Phenolic acids consist of gallic acid, caffeic acid, and chlorogenic acid. Meanwhile, flavonoids in tea encompass six subcategories, including anthocyanins, flavonols, flavanols, flavanones, flavones, isoflavones, and catechin derivatives [16]. Flavonoids are molecular structures with a

phenolic benzopyran configuration and are primarily present in plants, often in the form of glycosides. Additionally, other phenolic compounds such as phenolic acids, stilbenes, tannins, and lignans can be found in leaves, floral tissues, and woody parts of plants [17].

Flavonols are a subtype of flavonoids, with kaempferol and quercetin being the most commonly found in food sources. Flavones, on the other hand, are less common than flavonols and consist of glycosides, luteolin, and apigenin. Flavanones are present in human foods such as tomatoes and specific aromatic plants like mint [18]. Flavanones are typically glycosylated by disaccharides at the seventh position of neohesperidose, imparting a bitter taste as seen in citrus fruits [19]. Flavanols, which include catechins and proanthocyanidins, are another category of polyphenols. Catechins are a group of condensed tannins and are often referred to as polyphenols due to their numerous hydroxyl groups [20]. Catechins consist of epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC) [21]. Green tea contains approximately 200 mg of catechins, with the highest concentration belonging to epigallocatechin gallate (EGCG) at 60%, epigallocatechin (EGC) at 20%, epicatechin gallate (ECG) at 14%, and epicatechin (EC). Other compounds like quercetin, kaempferol, myricetin, flavonols, and flavones are present in lower concentrations [22]. Green tea is renowned as an excellent source of catechins. The antioxidant capacity of green tea leaves can vary significantly, depending on various factors such as variety and geographical origin [23]. Green tea, which undergoes minimal fermentation, contains the highest concentration of catechins, with EGCG reported to have antioxidant, anti-inflammatory, and anticarcinogenic effects [24]. The chemical structure depicted in Figure 1 consists of a condensed polyphenol ring with a six-membered oxygen-containing heterocyclic ring carrying the polyphenol ring at position 2. Catechins contain two hydroxyl groups at positions 3 and 4. The structural difference between EGC and EC is that EGC has an additional hydroxyl group at position 5 of the B ring. ECH and EGCG are ester derivatives of EC and EGC, respectively, formed through esterification with the gallic acid moiety at position three on the C ring [25]. Other components in tea, derived from non-flavonoid components, include carbohydrates, pectin, alkaloids, chlorophyll, proteins, various amino acids, organic acids, resins, vitamins, and minerals. It is the amalgamation of these elements that enhances the content of the tea, contributing to its unique flavor profile when consumed [26]. Green tea contains high levels of xanthine bases such as theophylline and caffeine, as well as pigments like chlorophyll and carotenoids. Phenolic acids present in green tea, such as gallic acid and proanthocyanidins, can influence the characteristics of tea. Phenolic acids also play a role in the formation of catechins [23].

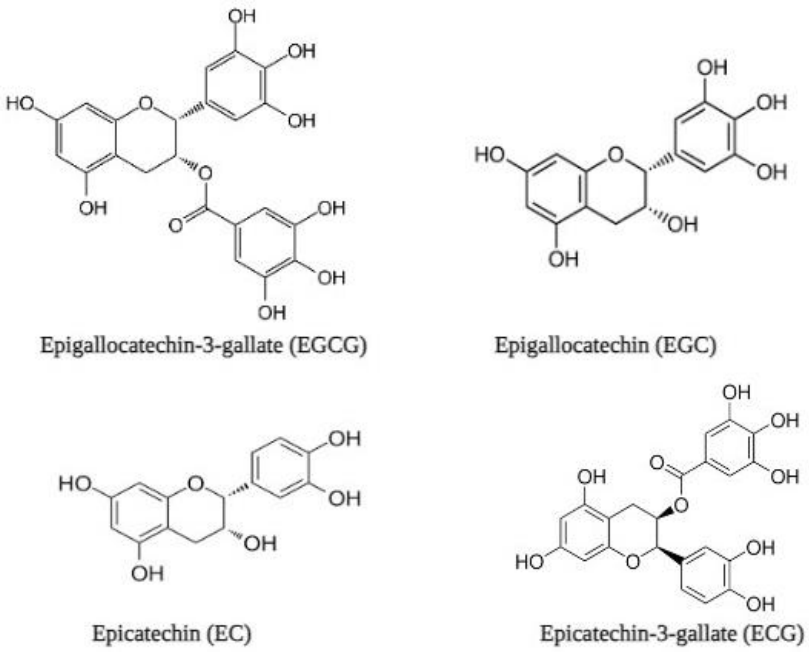

Figure 1. The structure of many types of catechins.

Proanthocyanidins, also known as concentrated tannins, are dimers, oligomers, and polymers of catechins linked by C4-C8 bonds. Proanthocyanidins are found in significant quantities in grapevines, primarily in the skin and seeds [27]. Tea contains vitamin A (beta-carotene), theobromine, carbohydrates, fats, and proteins in extremely minimal amounts, approaching nearly zero percent. Additionally, tea includes compounds such as caffeine, purine alkaloids, theophylline, theobromine, aglycone, baringtogenol C, triterpene saponin, kavalactone derivatives, theogallin essential oil, and linalool. Among the major secondary metabolites found in tea leaves are phenolic compounds [28].

The Benefits of Green Tea Polyphenols for Kidney Health

The antioxidant compounds in tea can inhibit the development of diseases caused by free radicals. Green tea contains various polyphenols that can have positive impacts on health. Experiments conducted through both in vivo and in vitro approaches, as well as clinical investigations, indicate that polyphenols possess antioxidant, anti-inflammatory, and cardiovascular properties. Catechins are the primary type of polyphenols found in green tea. The antioxidant properties of catechins enable them to bind to copper ions (Cu) in redox reactions and neutralize ROS [29]. Epigallocatechin-3-gallate (EGCG) can protect the kidneys from ischemia-reperfusion injury (blood vessel blockage) in the kidneys, kidney fibrosis, and it is involved in the inflammatory response. Catechins can function as antioxidants, anti-inflammatory agents, and anti-apoptotic agents, serving to safeguard kidney cells from damage [30]. Antioxidants can inhibit cell damage and provide benefits to the body. Tea polyphenols have been demonstrated to act as antioxidants in vitro by preventing ROS [31]. Several in vitro and in vivo studies have explored the potential benefits of green tea, particularly its major component, EGCG, in various kidney disorders. The antioxidant, anti-inflammatory, and anti-apoptotic properties of EGCG show promise as an alternative therapeutic approach to preventing kidney diseases [32]. EGCG has been demonstrated to protect the kidneys from iron-induced renal damage, acting as an iron chelator that forms stable complexes with iron ions and neutrophil gelatinase lipocalin (NGAL), consequently reducing the chemical reactivity of ROS [33]. Additionally, EGCG enhances kidney function and mitigates hypoxia and nitrosative stress-induced damage [34].

EGCG ameliorates acute kidney injury associated with heart bypass in diabetic rats. EGCG prevents renal tubular damage, reduces the levels of kidney injury molecule-1 (Kim-1), and mitigates neutrophil gelatinase lipocalin-induced kidney injury [34]. Administration of green tea supplements reduces the amount of calcium oxalate crystals in the kidneys of rats exposed to ethylene glycol, indicating protection against kidney damage [35]. EGCG can restore normal mitochondrial electron transport chain function in the kidneys of rats damaged by cisplatin [36]. In obstructive nephropathic rats, treatment with EGCG inhibits nuclear factor-kappa B activation [37]. EGCG induces the expression of glutathione-s-transferase (GST), glutathione peroxidase (GPX), and heme oxygenase-1 (HO-1), which are capable of removing ROS and oxidative stress [38]. Additionally, there are other compounds, such as resveratrol in polyphenols, that can combat kidney injuries.

The antioxidants in tea compounds can inhibit the growth of diseases caused by free radicals. Antioxidants are molecules that can donate their electrons to free radicals, thereby reducing free radicals through a chain reaction process. In the body, antioxidants play a crucial role in preventing oxidative stress, which can impede the development of diseases such as cancer, stroke, and coronary heart disease [39]. Additionally, green tea polyphenols can protect the kidneys of rats from oxidative damage caused by a high-fat diet through the sirtuin 3 manganese superoxidase dismutase (SIRT3/MnSOD) pathway by peroxisome proliferator-activated receptor alpha (PPARα) [36]. Polyphenols from apples have been reported to improve kidney fibrosis by reducing monocyte infiltration, thereby slowing down kidney obstruction [40].

Resveratrol is a trihydroxy derivative of stilbene obtained from various plants such as grapes, legumes, and fruits. The activity of resveratrol can act as an anti-inflammatory, antioxidant, antibacterial, anti-obesity, and anti-cancer agent [41]. Resveratrol is generally considered an efficient preventive measure against ROS and free radicals. This compound is reported to play a crucial role in kidney ischemia/reperfusion injury, particularly at the tubular level [42]. It can be found in plants and has been extensively studied for its potential to protect against acute kidney failure. Resveratrol has shown its effectiveness in combating acute kidney failure by targeting ROS in human kidney cells [43].

Other studies also indicate that EGCG compounds reduce ROS and kidney damage caused by excess iron, reduce hypoxia and oxidative stress [44]. Resveratrol effectively reduces ROS that occurs in kidney cells by reducing inflammation (TNF-α and IL-1β) resulting from kidney failure and restoring changes in apoptosis-related proteins [45]. Phenolic acid and gallic acid contained in plants also show significant protection against kidney injuries [46]. Therefore, polyphenols are considered to be highly suitable for use as a therapy in kidney repair.

The compound quercetin is abundant in fruits, vegetables, and leaves. This compound possesses strong antioxidant properties, reducing cell aging by diminishing oxidative stress. Quercetin prevents kidney damage and inhibits kidney inflammation in diabetic nephropathic animals. Treatment with this compound prevents structural and functional kidney tissue damage and suppresses oxidative stress in rats. Research has revealed that prolonged exposure to certain toxic substances or harmful pollutants can lead to nephrotoxicity [47]. Numerous experimental studies and explorations of transduction mechanisms and multifaceted signaling pathways suggest that quercetin holds significant potential in reducing kidney toxicity [48]. Quercetin exhibits chemoprotective and anti-apoptotic effects resulting from increased expression of p53, p21, and p27 and reduced Bax expression in vitro [49]. In rats treated with cisplatin, quercetin can reduce tubular injury, lower the regulation of pro-inflammatory mediators, and maintain kidney blood flow. Furthermore, quercetin also demonstrates antioxidant and anti-apoptotic effects [50].

Kaempferol induces a significant reduction in malondialdehyde (MDA) levels, which is a leading cause of oxidative stress, cytotoxicity, and kidney damage in calcineurin inhibitor-induced kidney injury. Treatment with kaempferol enhances GSH and superoxide dismutase 2 (SOD2) while reducing TNF-α and IL-6 levels in the kidneys of rats treated with doxorubicin [51]. Kaempferol exhibits a strong and broad inhibitory effect on end-stage kidney disease. It affects the gene expression associated with fibrosis in NRK-52E transformed cells through transforming growth factor beta 1 (TGF-β1). Therefore, kaempferol could be a promising candidate for treating kidney fibrosis [52].

Polyphenols such as catechin, ellagic acid, resveratrol, quercetin, curcumin, EGCG, and kaempferol offer protection against kidney injuries. They improve mitochondrial function by stimulating peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α), nuclear respiratory factor 1/2 (NRF1/2), and mitochondrial transcription factor A (TFAM), thus enhancing kidney function. Overall, polyphenols regulate the electron transport chain, support ATP formation, counteract free radicals, and inhibit protein and lipid oxidation in nephrotoxicity and kidney nephropathy [53].

In vitro studies demonstrate that epicatechin gallate inhibits the production of pro-inflammatory cytokines, such as IL-1β, and enhances the production of anti-inflammatory cytokines, such as IL-10, in human leukocytes. Pre-treatment with epicatechin gallate helps maintain glutathione at basal levels in kidney tissues [54]. Other research indicates that epicatechin gallate can scavenge free radicals and convert them into non-toxic products. Treatment with epicatechin gallate reduces the inflammatory response induced by cisplatin, leading to reduced cell death and kidney failure. In rats treated with cisplatin, epicatechin gallate significantly decreases NF-

κB activation, a transcription factor that activates pro-inflammatory cytokines like TNF-α and IL-6 in response to oxidative stress [55].

Mechanism of Action of Green Tea Polyphenols for Kidney Health

A growing body of evidence from epidemiological studies suggests that the consumption of polyphenols has the potential to impede the aging process and serve as a preventive and therapeutic measure for conditions like cancer, neurodegenerative diseases, cardiovascular issues, and cerebrovascular disorders [56]. Saponin compounds derived from tea seeds have the ability to restore capillaries to their normal function during episodes of inflammation, although it's worth noting that these saponins are only present in small quantities within tea leaves [57]. When polyphenolic compounds are introduced into the bodies of test animals, they reveal specific mechanisms by which tea polyphenols act as antioxidants. These mechanisms include enhancing the activity of antioxidant enzymes, preventing the oxidative degradation of fats, synergistically scavenging free radicals in conjunction with other nutrients [58], and reducing the oxidation that occurs when metal ions bind to molecules [59]. Together, these processes demonstrate the antioxidant properties of tea polyphenols. It's important to note, however, that certain compounds like catechins and teaflavins can potentially lead to increased production of ROS in the body [60].

Tea Consumption for Kidney Health

Tea is one of the most popular and widely enjoyed beverages worldwide [61]. It provides anti-inflammatory benefits, making it a dietary supplement and serving as a beverage [62]. The consumption of green tea has not been extensively studied in children, while in adults, the recommended intake varies based on the type of tea. Adult tea consumption is recommended at 2-3 cups per day, providing 240-320 mg of polyphenols or 100-750 mg per day from green tea extract [63]. Numerous studies have been conducted to explore the relationship between tea consumption habits and their potential impact on chronic kidney disease (CKD), estimating glomerular filtration rate (eGFR) thresholds, and investigating the connection between tea benefits and albuminuria, but the findings are quite limited [64]. Polyphenols can protect against chronic kidney failure by around 32% if consumed in moderate amounts (6.8 mg) [65]. Nonetheless, these studies have fallen short of providing definitive and accurate solutions, mainly due to the variations in tea types (such as green tea, black tea, and oolong tea) and individual characteristics [66]. However, recent research reports indicate that tea may offer positive effects on patients with metabolic syndrome (MetS) [67]. Chinese researchers have also found that oolong tea significantly improves eGFR efficiency when compared to green and black teas [68].

Side Effects of Tea Consumption

Tea is closely intertwined with daily human life, frequently enjoyed as a relaxing beverage in the afternoon or consumed after meals [69]. Various studies have reported that tea possesses antioxidant, thermogenic, anti-inflammatory, cholesterol-lowering, antimicrobial, neuroprotective, antihypertensive, and anticarcinogenic properties [70]. Tea also demonstrates favorable effects in combating various chronic diseases. However, amidst all these benefits, there are various side effects and contradictions associated with tea consumption. Excessive consumption of green tea can lead to numerous adverse effects. Chemical derivatives of green tea can cause acute hepatotoxicity [71]. Tea contains caffeine, which can result in insomnia and central nervous system stimulation, leading to symptoms such as nausea and vomiting [72]. One cup of black tea and green tea contains approximately 40 milligrams of caffeine. Despite having a lower caffeine content compared to a cup of coffee, excessive consumption can lead to

various sleep disturbances [73]. Individuals consuming large amounts of caffeine, including that from green tea, over an extended period may experience irritability, insomnia, diarrhea, headaches, and loss of appetite [74]. Recent research indicates that the consumption of large quantities of green tea can lead to several side effects, prompting experts to recommend limiting daily intake. Some of these side effects include heartburn and other gastroesophageal diseases [75]. The theophylline in green tea can induce acid reflux [76]. Excessive tea consumption can also lead to asymptomatic erosive esophagitis [77].

Conclusions

Tea polyphenols are highly beneficial for maintaining kidney health. Research has shown that polyphenols, particularly EGCG, can protect the kidneys from ischemic injury, kidney fibrosis, and prevent inflammatory responses. The numerous benefits of polyphenols, especially catechins, are highly advantageous for kidney health. However, recent studies have yielded somewhat inconclusive and inconsistent results, necessitating further research to provide more precise insights.

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