Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 3
BLSME 2024

Health Benefits of Tea Polyphenols and Mechanisms via Regulating Gut Microbiota

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Abstract. Tea has been a beloved beverage for centuries, enjoyed by people all over the world. Tea polyphenols, natural bioactive compounds abundant in tea, have gained increasing attention for their potential health-promoting properties. This study provides a comprehensive overview of the multifaceted interactions between tea polyphenols and gut microbiota, shedding light on their roles in health and disease prevention. The opening section provides an in-depth examination of the definition and categorization of tea polyphenols, and their prevalence in various types of tea. Subsequently, the following section conducts an extensive analysis of the crucial role played by gut microbiota and the ways in which tea polyphenols modulate their composition, including their potential as prebiotic agents. In addition, this paper discusses the diverse health-promoting aspects of tea polyphenols, such as their antioxidative properties, anti-inflammatory effects, and their potential impact on conditions like inflammatory bowel diseases (IBD) and colorectal cancer, furthermore, explores their role in addressing functional disorders like depression and combating fatigue. This paper highlights the intricate interplay between tea polyphenols and gut microbiota and underscores the potential significance of these interactions in promoting health, advancing the understanding of the role of tea polyphenols in wellness and disease prevention.

Keywords: Tea Polyphenols; Gut Microbiota; health-promoting; prebiotic agents.

1. Introduction

Studies on the health benefits of tea polyphenols have gained a lot of attention in recent years. In addition to being the most popular beverage worldwide (after water), tea has a substantial economic impact on the commercial sector and is among the world's oldest drinks, according to research from the Food and Agricultural Organization of the United Nations. It has a rich history and cultural significance. The location of tea leaf harvesting, cultivation, and processing techniques, such as fermentation and drying, all affect the tea's flavour. Each type of tea boasts its unique flavor, aroma, and health benefits, making it a highly prized commodity and an integral element of social connections [1]. In addition to its cultural significance, tea has gained considerable attention due to its high polyphenol content, which holds the potential for therapeutic benefits for the general population [2,3]. The multifaceted health-promoting properties of tea polyphenols are well-documented, encompassing their roles as antioxidants, anti-inflammatory agents, anticancer compounds, mood enhancers, fatigue reducers, cholesterol regulators, anti-obesity agents, anti-aging elements, antidiabetic agents, antibacterial substances, immune system regulators, metabolic modulators, and contributors to cardiovascular and cerebrovascular health. This study offers a comprehensive overview of the latest research findings on the diverse health benefits of tea polyphenols, as well as their interactions with gut microbiota. Additionally, it briefly discusses the fermentation process of tea and its impact on the composition of polyphenols.

2. Overview of Tea polyphenols

2.1. Definition and Role in Tea

Tea polyphenols (TPs) are the general name for polyphenols in tea, which are the key compounds contributing to the color, flavor quality and efficacy of tea leaf-derived products, accounting for 18% to 36% of the dry weight of tea [3]. The polyphenolic compounds that fall under the category of flavonoids, anthocyanins, anthocyanidins, flavanols (catechins), and phenolic and deps phenolic acids are the most important. Among them, catechin content is the highest, besides, it is the main ingredient of health-care functions. There are four categories into which catechins can be separated: (-)-epicatechin-3-gallate (ECG), (-)-epigallocatechin (EGC), (-)-epicatechin (EC), and (-)-epigallocatechin-3-gallate (EGCG) [3, 5]. It is commonly known that flavonoids are antioxidants that may stop radical chain reactions and neutralize free radicals [6]. Whereas anthocyanins may be found as acylated anthocyanins and anthocyanidin glycosides, anthocyanidins can be found as 3-hydroxyanthocyanidins, 3-deoxyanthocyanidins, and O-methylated anthocyanidins. Anthocyanins are colored pigments that dissolve in water; they look red in acidic environments and change blue in alkaline ones. Copigmentation and temperature are two factors that affect anthocyanin color change [7]. The last class of aromatic compounds includes phenolic acids, which are made up of hydroxyl and carboxyl groups in their molecules [8].

2.2. Fermentation Levels and Tea Polyphenol Content Found in Different Tea

The polyphenol content in tea leaves, particularly the catechin component, can undergo changes during the tea manufacturing process, influenced by fermentation and heating processes [9]. Broadly, tea can be categorized into three types based on the degree of fermentation: green tea, oolong tea, and black tea [4]. Green tea is produced from dried tea leaves and contains significantly higher levels of polyphenols, as it does not undergo the fermentation process. Consequently, green tea polyphenols (TPs) have higher quantities of oligomeric polyphenols. Among these, catechins constitute approximately 59% of the total, with EGCG (epigallocatechin gallate) being the most abundant polyphenol in green tea. To prevent the oxidation of tea catechins, fresh tea leaves are rapidly heated and dried, deactivating polyphenol oxidase and native microflora [9, 10]. Black tea is fully fermented or heavily oxidized. Its TPs are generated through a process known as "tea fermentation," which involves the enzymatic oxidation of tea catechins in crushed, withered tea leaves, aided by polyphenol oxidase and peroxidase enzymes [10,11]. Subsequently, the tea leaves are dried and roasted to deactivate these enzymes. This oxidation process reduces the astringency and bitterness associated with high catechin levels [12]. Oxidized products of polyphenols derived from tea leaves (Camellia sinensis) are collectively referred to as tea pigments, primarily including theaflavins (TFs), thearubigins (TRs), and theabrownin (TB) [11]. The process of oxidation transforms catechins into polymeric thearubigins and dimeric theaflavins, which give black tea its unique flavor and color. The two main catechins found in black tea are EGCG and ECG (epicatechin gallate) [9]. Most polyphenols' oxidation is impacted by the pseudo-first-order kinetics of fermentation [5]. In terms of degree of fermentation, oolong tea is in between green and black tea. This semi-fermented tea contains both high-molecular-weight theaflavins and monomeric catechins. Procyanidins (condensed tannins) are found in both fresh and oolong tea. They are made up of oligomers and polymers of flavan-3-ol molecules. Since they are less stable, highly polymerized flavan-3-ols are found in black tea less frequently [9].

3. Gut Microbiota-Tea Polyphenols Interactions

3.1. Gut Microbiota

The gut microbiota, encompassing a diverse array of microorganisms in the gastrointestinal tract, forms a complex ecological community that significantly influences the health of the host. This microbial community, totaling around 100 trillion microorganisms, is predominantly constituted by bacteria, but also includes viruses, protozoa, and eukaryotic fungi. The major bacterial phyla in the intestinal microorganisms comprise actinobacteria, Proteobacteria, Verrucomicrobia, and Fusobacteria [13]. Fundamental processes such as digestion, metabolism, and vitamin production in animal bodies are heavily reliant on the presence and activity of the gut microbiota [14].

Within the intricate microbial community of the human intestinal tract, there exist beneficial bacteria, potentially harmful bacteria, and other bacteria with dual effects. Among the potentially harmful bacteria are strains such as Clostridium, Staphylococcus, and Veillonella, which have the capability to produce harmful substances, associated with intestinal diseases and other immune-related disorders [13]. Conversely, beneficial bacteria, predominantly Lactobacillus and Bifidobacterium, act as antioxidants. They regulate oxidative stress reactions in metabolism, reduce gas production, generate short-chain fatty acids (SCFAs), stimulate the immune system, and exhibit anti-tumor activity. Playing a pivotal role in nutrition and disease prevention, these beneficial bacteria are often employed as probiotics. In summary, the gut microbiota critically maintains immune and metabolic balance and provides protection against pathogens [13].

Comprehending the intricate connections between the host and the intestinal microbiota is pivotal to unravelling the microbiota's role in biological processes and its influence on health and disease development. The diversity of microbes, reflecting the array of species in the community, tends to decrease in the face of gut dysbiosis. Conversely, a wealth of species is often associated with a "healthy gut" [15]. The gut microbiota has the capability to generate enzymes facilitating the breakdown of polysaccharides and plant polyphenols, as well as the synthesis of certain vitamins, thereby contributing to the intestinal well-being of the host [14]. A state of harmonious equilibrium among bacteria is maintained within a healthy gastrointestinal system, where genetic and environmental factors play a role in determining the type, quantity, and proportion of gut microbiota. The structure, composition, and quantity of the intestinal microbiota exhibit variability. Under normal circumstances, a symbiotic relationship prevails between the gut microbiota and the human body, holding significant importance in sustaining immune function and metabolic balance [13]. Dysbiosis, or an altered gut bacterial composition, has been linked to the pathogenesis of numerous inflammatory diseases and infections. Therefore, strategies aimed at preventing and treating such conditions involve accurately restoring the balance of the intestinal microecology [14].

3.2. Tea Polyphenols Modulating Gut Microbiota As Prebiotics

The intricate relationship between the metabolism and absorption of TPs and the involvement of intestinal microbiota results in metabolites that have positive effects on both the intestinal microbiota and the overall body. This is achieved by reinforcing the defensive capabilities of intestinal epithelial cells and regulating the composition of the intestinal microbiota. TPs are crucial in positively regulating the animal intestinal mucosal barrier, serving as a defense system against external infections. This helps maintain intestinal homeostasis and promotes the balance of the intestinal microbiota for overall body health [14]. Similar to established prebiotics, TPs influence the composition of gut microbiota and contribute to the formation of health-promoting metabolites [16]. Notably, catechins showcase prebiotic-like activities, rendering them apt as functional food ingredients to prevent imbalances in gut microbiota. In essence, TPs can be considered as an additional source of prebiotics [2].

Most TPs pass through the small intestine unaltered and get in the large intestine undamaged. A wide variety of microorganisms, primarily anaerobic bacteria, live in the intestinal lumen [16]. The gut microbiota has the ability to break down non-bioavailable or indigestible dietary ingredients, such as TPs, in the small intestine by utilizing their diverse metabolic capacities. A variety of short-chain phenolic acids (SCPAs), often referred to as (hydroxylated) phenylcarboxylic acids, are produced as a result of their microbial degradation. In the colon, these resultant SCPA metabolites are more easily absorbed. Moreover, SCPAs have a number of positive impacts on systemic health, regulating important metabolic processes such platelet aggregation, the activity of the angiotensin-converting enzyme, the oxidation of erythrocytes and low-density lipoproteins, and cytotoxicity caused by oxidative stress [16].

In addition, current research on the regulation of intestinal flora by TPs mainly focuses on its dual effects: inhibiting the growth of dysfunctional intestinal flora and promoting the proliferation of beneficial microorganisms [14]. TPs can increase the activity of trypsin, thereby activating proteases in the stomach and small intestine and accelerating the decomposition and absorption of food. In particular, tea phenols help increase overall microbial diversity and adjust the structure of the gut microbiota. This is achieved by increasing the concentration of probiotic lactobacilli such as Enterococci, Lactobacilli and Bifidobacteria while reducing the abundance of potentially pathogenic bacteria such as Escherichia, Helicobacter pylori and Staphylococcus aureus. Therefore, this helps maintain a healthy and stable intestinal micro-ecosystem [14,15]. Findings from diverse in animal experiments and clinical case studies indicate that TPs possess the ability to enhance probiotic growth, selectively hinder the growth of pathogenic bacteria, fine-tune the composition of the intestinal microbiota, and modulate the balance of the intestinal microecology [14,16].

4. Health-promoting Properties of Tea Polyphenols and Specific Mechanisms

4.1. Antioxidant

TPs are natural antioxidants found in tea leaves. The mechanisms involve scavenging free radicals, increasing the activity of antioxidant enzymes, inhibiting lipid peroxidation, and reducing oxidation through metal ion chelation [17]. These processes work together to produce the overall antioxidant effect [4].

Free radicals, which are highly reactive molecular byproducts of cellular respiration and metabolic processes, can have both physiological and pathological effects. Reactive oxygen species (ROS) are closely linked to these events. At low levels, ROS can act as signaling molecules that regulate important cellular activities such as cell growth and adaptive responses. However, when the balance between ROS accumulation and the body's antioxidant defense mechanisms is disrupted, it leads to oxidative stress and damage to cells and tissues [4]. TPs have the ability to interact with ROS, forming stable phenolic oxygen radicals that help eliminate free radicals. Metabolites of TPs also possess antioxidant properties. The effectiveness of tea polyphenols in scavenging ROS depends on factors such as the number of hydroxyl groups in their structure, the surrounding environment, and the stability of phenolic oxygen radicals [4]. In addition to their direct scavenging abilities, TPs also protect the body from oxidative damage by regulating the activities of various oxidase and antioxidant enzymes [4]. Moreover, certain transition metal elements catalyze specific oxidation reactions within the body, resulting in the production of a substantial number of free radicals. Tea polyphenols inhibit the initiation of these oxidative processes through cation chelation [4].

Advanced glycation end products (AGEs), also known as glycotoxins, are potent oxidant compounds that contribute to oxidative stress and inflammation. They are the outcome of a non-enzymatic interaction between free amino groups in proteins, lipids, or nucleic acids and reducing sugars [18]. Age-related diseases, liver disorders, neurodegenerative conditions, and microbiome-related illnesses are all significantly influenced by AGEs and their cell surface receptor (RAGE) [18]. The pathogenic circumstances caused by AGE-RAGE are primarily driven by three mechanisms: oxidative damage, inflammation, and the activation of fibrogenic signaling pathways [19]. Precursors for the production of AGEs are reactive carbonyl species (RCS), which are created during thermal processing from carbohydrates [18]. Scavenging RCS proves to be an effective strategy to prevent AGE formation, and tea polyphenols have demonstrated efficiency as scavengers of RCS owing to their antioxidant activity and their capability to attack electron-deficient RCS to form adducts [19].

4.2. Anti-inflammatory

TPs undergo absorption, metabolism, and distribution within the body. Unabsorbed polyphenols can bind to immune cell surfaces and enterocyte receptors, effectively blocking pro-inflammatory signals. Both the polyphenols that remain unabsorbed and their resulting metabolites have the potential to positively influence local inflammation or serve as prebiotics, promoting the growth of beneficial microbes and contributing to enhanced gut health. Several investigations have demonstrated the anti-inflammatory characteristics of dietary TPs, which include direct antioxidant action, induction of cytoprotective mechanisms, and inhibition of pro-inflammatory signal transduction [9].

4.3. Inflammatory Bowel Diseases (IBD) and Colorectal Cancer

Numerous illnesses can begin as a result of prolonged or uncontrolled inflammation. Crohn's disease and ulcerative colitis are included in the category of inflammatory bowel disease (IBD), which is defined by recurrent and persistent inflammation. TPs have been shown to have anti-inflammatory and antioxidant properties, which help in IBD treatment. These polyphenols strengthen cytoprotective defense systems and differently regulate gene expression to reduce oxidative/nitrosative stress, inflammation, and cell damage. Tea polyphenols have been proved to be a successful therapy and preventative method for intestinal inflammation and related damage [9].

The hypothesis that alterations in the gut microbiota precede the development of inflammatory bowel disease (IBD) is robustly supported by several study findings [20]. The integrity of the intestinal barrier may be jeopardized by disruptions in the gut microbiota, which can lead to a decrease in the production of tight junction proteins. As a result, this disintegration permits more microorganisms and/or microbial molecular patterns to get through, which in turn sets off an increase in innate and adaptive immune responses as well as inflammation. Furthermore, the imbalance of gut microbiota can be further disrupted by the proinflammatory and prooxidant profiles that define inflammatory conditions in the gastrointestinal tract, which can lead to unfavorable clinical outcomes [9]. In the gastrointestinal (GI) tract, bacteria ferment undigested carbohydrates to create short-chain fatty acids (SCFAs). In addition to providing energy, SCFAs are necessary for the digestion of indigestible polysaccharides, the synthesis of certain vitamins, the protection of the intestinal mucosa, and the inhibition of the proliferation of harmful microbes [2]. SCFAs support intestinal epithelial cells with energy, suppress inflammatory signaling pathways, and increase the production of tight junction proteins, which strengthen the epithelial barrier and protect colon health and reduce colitis [2]. Notably, individuals with IBD have been found to have gut dysbiosis, an imbalance in the gut microbial population marked by a marked decrease in bacteria that produce fatty acids (SCFAs). Both the onset of colorectal cancer and the aggravation of IBD are facilitated by this dysbiosis [9, 20]. Tea polyphenols have been shown to have a positive effect on colitis, which may be partially attributed to their capacity to improve intestinal dysbiosis. As stated before, the polyphenols found in tea have the ability to suppress bad bacteria and function as prebiotics, encouraging the growth of good bacteria and improving the balance of microbes in the gut. Epigallocatechin-3-gallate (EGCG), one of the main bioactive polyphenols in green tea, has anti-inflammatory and antioxidative qualities. According to research, taking EGCG orally can reduce the symptoms of clinical colitis, lessen colonic damage, reduce oxidative stress, improve the function of the damaged mucosal barrier, and alter the composition and SCFA production of the gut microbiota [20]. The result of these changes in gut microbiota is an increase in the synthesis of protective SCFAs such butyrate. This ultimately leads to a notable reduction in intestinal inflammation and damage by inducing an anti-oxidative, anti-inflammatory, and barrier-enhancing response [20].

In order to maintain host homeostasis, the intestinal epithelial barrier—a single-cell layer that divides host components from the outside world—is essential. Tight junction proteins are essential for preserving epithelial barrier functions and for preserving the integrity of the gut barrier. Tight junction proteins are downregulated in diseases such as inflammatory bowel disease (IBD), which increases the permeability of the gut to bacteria, microorganisms, and toxic metabolites. This, in turn, sets off systemic inflammatory reactions. As stated before, tea polyphenols has the capability to improve the integrity of the epithelial barrier, thereby producing positive effects on IBD.

4.4. Depression

Feelings of hopelessness, lack of joy or motivation, guilt, low self-worth, poor appetite, sleeplessness, exhaustion, and trouble focusing are all signs of depression. Regular tea drinking is strongly positively correlated with a lower risk of major depressive disorder (MDD). A reduced incidence of depression has been linked to increased tea drinking, according to a meta-analysis of 11 studies with 13 reports [2].

The hypothalamic-pituitary-adrenal (HPA) axis, often referred to as the "stress circuit," influences mood and operates as a feedback loop. HPA axis hyperactivity, resulting from a lack of responsiveness to negative feedback or prolonged stress, can lead to continuous stress circuit operation and potentially contribute to depressive symptoms. In cases of HPA hyperactivity, the body increases cortisol release, paradoxically leading to more stress and inflammation. Tea polyphenols, particularly in green tea, have been shown to reduce glucocorticoids and adrenocorticotropin, decrease immobility in stress tests, and restore HPA activity through extracellular regulated protein kinase upregulation. Additionally, the aroma of green tea and black tea can lower CgA levels following stress load tasks. Overall, tea polyphenols have demonstrated the ability to normalize stress-induced HPA activity and provide antidepressant effects [2].

The monoamine hypothesis suggests that disruptions in the neurotransmission of monoamines such as serotonin, norepinephrine, and dopamine may contribute to depression. These monoaminergic systems can be influenced by specific gut microbiota species, forming the gut-brain axis. Short-chain fatty acids (SCFAs), elevated by tea consumption, can permeate the blood-brain barrier and have demonstrated antidepressant effects in mice. Modulations induced by tea polyphenols in Lactobacillus, Bifidobacterium, and Enterococcus species potentially contribute to improvements in monoaminergic systems, HPA axis activity, and brain-derived neurotrophic factor following tea consumption. Tea polyphenols and aromatic compounds in tea influence gut microbiota strains known as "psych biotics," which beneficially modulate the gut-brain axis, contributing to improved mental health and alleviation of depression [2].

4.5. Fatigue

Fatigue has emerged as a widespread health concern in contemporary societies across the globe. The development of fatigue-related conditions can be influenced by changes in the gut microbiome, and the physiological changes brought on by fatigue can also have an impact on the intestinal environment, changing the types and abundance of microbiota and increasing an individual's susceptibility to variations in microbiota. Certain polyphenols have shown notable effectiveness in reducing tiredness, including tannin, TPs, curcumin, and soybean isoflavones [13]. Studies have indicated that intestinal fermentation is a mechanism by which the gut bacteria might convert these active substances into even more powerful metabolites. Even while TPs are difficult to directly digest, the gut microbiota in the human intestine may break them down and metabolize them to produce more active metabolites like urolithin and equol. These metabolites contribute to the promotion of Lactobacillus and Bifidobacterium growth, potentially leading to improvements in gut microbiota composition and a reduction in fatigue [13]. The mechanisms underlying the anti-fatigue properties of polyphenols primarily center around their antioxidant and anti-inflammatory effects, the safeguarding of intestinal integrity, the regulation of energy metabolism, and the generation of anti-fatigue metabolites.

By enhancing the relative quantity, variety, and activity of favorable gut bacteria or by reducing the quantity or activity of harmful bacteria, TPs can reduce tiredness. This ultimately leads to the generation of advantageous SCFAs, intestinal barrier fortification, immune system strengthening, and the reduction of fatigue-related damage [13].

5. Conclusion

The potential health advantages of TPs linked with the gut microbiota are attributed to the combined actions of intact TPs and their microbial metabolites, which include gut barrier protection, probiotic control, anti-oxidation, and anti-inflammatory activities. The balance of gut microbiota can be influenced by various factors, including dietary choices, age, medication, environmental factors, and lifestyle. An imbalanced gut microbiota is a significant contributor to the onset and progression of numerous illnesses in the human body. Fatigue, oxidative stress, inflammation, and impaired intestinal barrier function are some of the adverse consequences associated with gut microbiota imbalance. Tea polyphenols possess anti-inflammatory and antioxidant properties that promote overall health and have therapeutic potential for disorders related to inflammation. The evidence supporting the role of tea as a chemo preventive agent against various malignancies continues to grow. With fewer side effects compared to conventional medications, tea polyphenols may emerge as a groundbreaking option for disease prevention and treatment. A thorough comprehensive understanding of these health benefits and the mechanisms by which TPs and their metabolites exert their effects is critical for the development of food or dietary interventions aimed at improving intestinal health and the overall well-being of the host.

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