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REVIEW ARTICLE

A glimpse through the origin, composition and biomedical applications of green tea and its polyphenols: A review

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Abstract

Green tea is an aromatic healthy beverage that is the least processed type of tea, containing numerous bioactive components beneficial to humans. It is produced from the plant *Camelia sinensis,* a shrub native to Asia. This article reviews the literature review on the origin, manufacturing, composition, biomedical applications and health benefits of green tea and its polyphenols. The main bioactive components of green tea are polyphenols, primarily flavonoids. Catechins are the main flavonoids present in tea. These high-potential compounds can stimulate certain enzymes and alter cellular functions by preventing the oxidation of biomolecules due to their antioxidant properties. The catechins found in tea include (-) –epicatechin (EC), (-) epigallocatechin (EGC), (-)-epicatechin-3-gallate (ECG) and epigallocatechin -3-gallate (EGCG). Epigallocatechin gallate (EGCG) is the most prominent catechin in fresh leaves, constituting around 50-60 % of the flavonoids. EGCG is the active component with significant health benefits. These catechins contribute to therapeutic actions and the prevention of infections. Recent research on green tea suggests various applications based on its medicinal value to reduce the risk of many diseases.

Keywords

Flavonoids; polyphenols; antioxidant; health benefits

Introduction

Tea is a widely consumed aromatic healthy beverage. It is the most consumed drink after water, according to data from the International Institute of Sustainable Development. Tea plants are native to East Asia, particularly China. China is the largest producer of green tea, accounting for 40 % of the world's tea production, with an annual output of 480000 tonnes and is also the world's largest exporter. Other major tea-producing countries include India, Kenya, Sri Lanka, Vietnam and Indonesia. Tea is an evergreen flowering plant best grown in tropical and subtropical regions (1-3). This review article provides an overview of the origin, composition, manufacturing process and health benefits of green tea catechins.

Origin and history of tea

The earliest credible record of tea consumption dates back to 2737 BC in China during the reign of Emperor Shen Nung. Being an herbalist, Shen Nung decided to utilize the infusion prepared when some dry leaves accidently fell into the drinking water boiled by his servant. The Chinese recog-

nized the importance of tea as a health-promoting agent to prevent certain illnesses and have used it as medicine for past 4000 years. This was recorded in an ancient book on medicine, Shen Nung's "Herbal classic" (1-3). Shen Nung is considered the "Legendary Father of Tea" (4). During the 300 years of the Tang dynasty (618-907 AD), the tea industry underwent a rapid revolution, was documented in the Ch'a Ching or "Tea Classic", written by Lu Yu of the Tang dynasty. It is one of the oldest books on tea in the world. An ancient Chinese proverb says "Better to be deprived of food for 3 days, than tea for one" (5).

Tea is produced from plants of the genus *Camellia* in the Theaceae family (4). Tea plants thrive in tropical and subtropical regions with adequate rainfall. All types of teas are harvested from *Camellia sinensis* and *Camellia assamica* (6, 7). The name "tea" is derived from the French word 'tisane' meaning an aqueous infusion of any herb. The tea plant is a perennial shrub that can reach a height of 2 m and live up to 70 years. The leaves are elongated, oval-shaped, with serrated edges and a dark green colour (Fig. 1). Economic production of leaves from a tea plant begins about 3-7 years after cultivation (8, 9). Tea is known for its rejuvenating and refreshing properties, with a soothing aroma. It possesses a wide range of physiological and pharmacological characteristics that make it useful for the prevention of diseases and infections. Darjeeling and Assam are the major tea-producing regions in India.

Fig. 1. Tea leaf.

Different types of tea

Tea is classified based on the degree and nature of the fermentation process into green tea, oolong tea, white tea, black tea, kukicha tea and pu-erh tea (9, 10). The first 4 types differ in the chemical changes and enzymatic oxidation during processing (Fig. 2).

Green tea is a non-fermented type of tea made from mature young leaves. It is quickly heated after harvesting, either by steaming or dry cooking, to reduce oxidation. As it is the least processed, it contains the most potent polyphenols (5). Green tea has a significantly higher concentration of antioxidant catechins compared to black tea, containing 4 times more. Minimal oxidation during processing preserves these catechins. Epigallocatechin gallate is a potent polyphenol that acts against free radicals. The astringency of green tea, a unique property, depends on its catechin content (5).

White tea is lightly fermented. The young leaves and buds are steamed to inactivate polyphenol oxidase and then dried (5, 6).

Oolong tea is semi fermented, with its composition intermediate between green tea and black tea. It is 8-85 % oxidized, containing a mixture of non-oxidized monomeric polyphenols and high molecular weight theaflavins. The name "Oolong" is derived from the Chinese word "Wulong", where 'Wu' means black and 'Long' means dragon. Originating in the Fujian province of China, oolong tea leaves are dried and roasted in multiple steps until they are dark and curled, resembling a black dragon. Oolong tea has higher gallic acid content and less EGCG compared to other teas. It improves in tastes when stored for a longer period and is renowned for its aroma and astonishing flavour (11).

Black tea is fully fermented (9, 10). During this process, tea undergoes full oxidation, which alters the catechin content and results in the formation of theaflavins and thearubigins, compounds responsible for its black colour and distinct flavour (5). It is processed from catechins through the fermentation of flush, leading to various biochemical changes. Black tea contains tannins, which inhibit the absorption of iron (12). The aerobic oxidation of catechins during black tea manufacturing is catalysed by the enzyme polyphenol oxidase present in tea leaves.

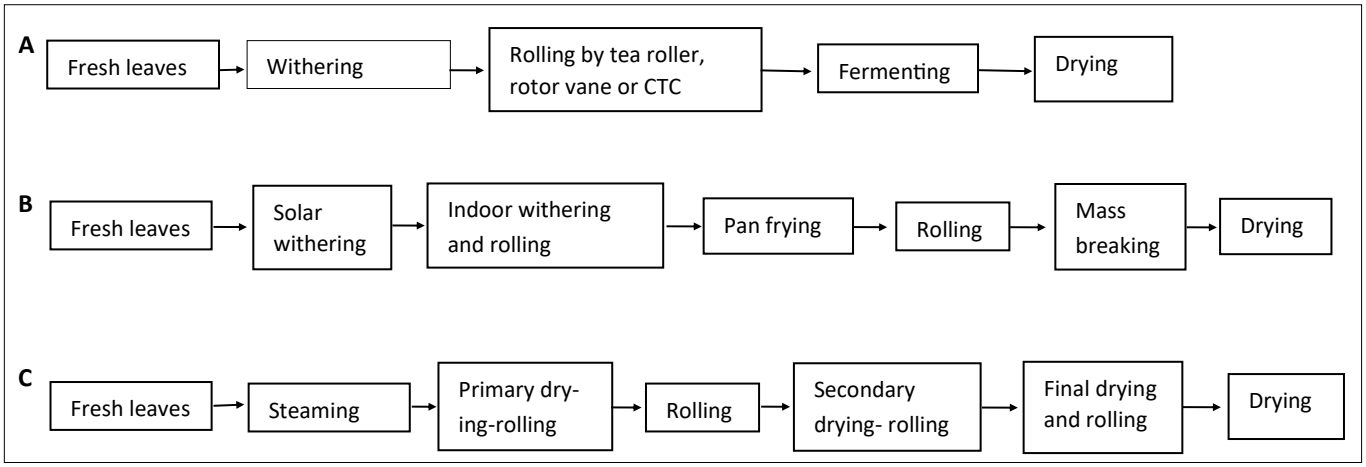

Fig. 2. The processing of tea: (**A**) black tea, (**B**) oolong tea and (**C**) green tea.

This process gives black tea its unique taste and colour (10). Black and green tea is the most popular types of tea consumed, with green tea having more demand due to its health benefits (13). Kukicha, also known as Twig tea, is a variety of tea prepared from the twigs and stems of *C. sinensis* (5, 6).

Pu-erh tea is manufactured from the leaves of the tea plant found in the Pu-erh district of Yunnan Province, China. This tea has gained popularity due to its medical benefits, such as antioxidant and hypolipidemic effects and is an agricultural product of geographical indication. Another form of Pu-erh tea, known as Pu-erh ripe tea, is processed through microbial fermentation (9, 14, 15).

Herbal teas are infusions or decoction of herbs, spices or other plant materials added to tea (6). One example is cacao tea, which contains a large amount of theobromine (6 %) and is obtained from *C. ptilophylla* (12).

Classification of green tea

There are various types of green tea based on taste and antioxidant properties, primarily produced in Japan and China. The most common Japanese type of green tea is Sencha, while other teas like Bancha, Matcha and Gyokuro are also prepared from Sencha (16).

Sencha – meaning "brewed tea" in Japanese, Sencha is widely grown in Japan in sunlight. It is prepared from young tea leaves by infusion and can be sweet or bitter with a fragrant aroma (16).

Matcha – A green tea powder rich in antioxidants, Matcha is highly popular in Japan. The tea leaves are ground into a fine powder and infused in hot water. It has a green colour with an umami flavour and vegetal taste. Matcha infusions contain higher amounts of L-theanine and caffeine (16).

Bancha – Made from older leaves and prepared from the last harvest. It contains less caffeine and L-theanine than Sencha, making it suitable for those who are sensitive to caffeine. It is beneficial for digestion and often enjoyed after meals (16).

Genmaicha – Also known as brown rice tea or popcorn tea. It is green tea mixed with roasted rice grain. It is low in caffeine, making it suitable for people sensitive to caffeine and it also provides the benefits of rice (16).

Gyokuro – Known as "pearl of dew" or "precious dew". It is one of the most refined teas grown on the island of Kyushui in Japan. It is cultivated in the shaded regions and has fine, needle-shape leaves. Harvested in the spring season, it offers a tender taste (16).

Most common Chinese types of green tea are Gun powder, Long jing, Chun mee and Mao feng.

Gun powder – Named for its distinct rolled shape, Gunpowder has a bitter and spicy flavour, making it suitable for preparing mint tea.

Long Jing – Harvested in the spring season in the Zhejiang region of China. It is rich in antioxidants and contains many detoxifying agents.

Chun mee – One of the popular types of tea produced in the Jiangsu province of China. It is slightly more acidic and astringent than other Chinese teas. It is often mixed with ginger, lemon, almond and jasmine for added flavor.

Mao feng – Also produced in the Jiangsu province of China. It has a sweet flavour and a refreshing taste (16).

Green tea manufacturing

The manufacturing process starts with the journey from the leaf to the cup. Two fresh leaves and a bud, known as a 'flush', are picked from the shrub. These are then macerated and heat-dried. The beverage is prepared by infusing the processed leaves in boiling water (5, 6). The process of making tea from tea leaves and hot water is called steeping or brewing. Steeping temperatures range from 61 °C to 87 °C, with a steeping period of 30 seconds to 3 min. Higher quality teas, such as Gyokuro, are prepared by steeping more tea leaves multiple times for short duration (6, 7). Oxidation is avoided in green tea to preserve its green colour and flavour (10).

There are 2 different types of processing methods. In the Japanese method, fresh tea leaves are steamed at 100 °C to inactivate the oxidizing enzymes, then rolled and dried. In the Chinese method, tea leaves are pan-fried at 300-350 °C to prevent oxidation. The green colour is maintained since the inactivated enzymes do not decompose chlorophyll. In China, some green tea undergoes a withering process, followed by rolling, drying and sorting (6, 10, 13).

Fermentation of Tea

It process begins with plucking the tea leaves and spreading them out in thin layers in a step known as withering. This allows the leaves to lose moisture in a balanced way, becoming pliable. Losing too much moisture results in a loss of flavour, while losing too little makes the leaves difficult to process.

The next step is pan drying or steaming, also known as fixing. Pan drying is done in large pans, which helps maintain the green colour and inhibit oxidation.

Rolling – In this step, the leaves are rolled to give them their characteristic shape. This break down the cell structure of the leaves, helping to release flavour during brewing.

Drying – This step further reduces moisture content, enhances flavour and provides a longer shelf life. However, drying at very high temperature can decrease catechin content and cause a loss of green colour.

Sorting and grading – The dried leaves are then sorted and graded based on their size and quality.

Composition of green tea

Green tea contains around 4000 bioactive compounds, (6, 9, 16) with polyphenols being the major ingredient. Among these, flavonoids are the most significant polyphenols (2, 5). Flavonoids (Latin: Flavus- Yellow) are yellow pigments in plants responsible for the colour of leaves, flowers and fruits. In 1936, Albert Szent-Györgyi discovered flavonoids in lemon peels (8).(Table 1.)

Table 1. Chemical composition of fresh green tea leaves (5, 14).

Component	Dry weight %
Polyphenols	25-35 %
Carbohydrates	5-25 %
Proteins	15 %
Caffeine	3.5 -4 %
Amino acids	1-4 %
Lignin	6.5 %
Lipids	2 %
Organic acids	1.5 %
Ash	5 %
Theanine	4 %
Chlorophyll	0.5 %
Theobromine	0.15-2 %
Theophyline	0.02-0.04 %
Minerals	

Catechin is the most important flavan-3-ol, a type of flavonoid, which belongs to a subgroup of naturally occurring phenols. Green tea has a higher amount of catechin than other teas. The name catechin is derived from the word 'catechu', referring to the boiled extract or tannic juice of *Mimosa catechu* (17). The leaves of the tea plant are rich in polyphenols, which makes up 10-15 % of the plant's weight. Catechins, the main flavonoids (polyphenol), constitute up to 25 % -30 % of the dry leaf weight (3, 18). Higher amounts of catechins are found in young leaves up to the 7th leaf compared to older leaves. Tea leaves contains an active enzyme polyphenol oxidase, which catalyses the aerobic oxidation of Catechins during the manufacture of black tea (5, 18-21).

EGCG is the most prominent catechin in fresh leaves, constituting around 50-60 %. The major catechins present in green tea are catechins (C), epicatechin (EC) 6 %, gallocatechin (GC), epigallocatechin (EGC) 20 %, epicatechingallate (ECG) 14 %, epigallocatehingallate (EGCG) 60 % and gallo catechin gallate (GCG) (5, 18, 22-24). These phenolic compounds play a major role in combating free radicals that cause diseases and in the prevention and treatment of various infections. Besides the natural amount of polyphenols in tea leaves, the concentration of polyphenols in tea is significantly affected by the age of the tea leaf, the infusion process, water temperature, the amount of tea used per cup and the brewing time (2, 5, 10, 18).

Basic structure of flavonoids

Flavonoids have a similar structure consisting of 15 carbon atoms arranged in 3 rings, forming the structure C6-C3-C6, also known as 1, 3 diphenylpropane. This structure is composed of 2 benzene rings (A and B) connected by a heterocyclic oxygen ring (7-9, 25) (Fig. 3-5). The concentration of catechin depends on the age of the leaf, with buds and young tea leaves containing the maximum amount (19). Tea also contains other flavanols such as quercetin, kaempferol, myricetin, as well as glycosides and depsides like chlorogenic acid, coumarylquinic acid and theogallin (3- galloyl quinin acid). Additionally, tea contains various minerals, vitamins and enzymes (3, 19, 26) (Fig. 6).

Catechins, the main astringency component in tea, were first isolated in 1929 by Dr. Michiyo Tsujimura at RIKEN, the institute of physical and chemical research in Japan (27). Normal catechins are colourless in aqueous solution but becomes orange or red, giving oolong tea and black tea their reddish colour (22). Carbohydrates, primarily in the form of cellulose, are one of the main components in tea (10). Enzymes such as polyphenol oxidase and peroxides, which are protein, responsible for the oxidation of catechins during the processing of black tea (10). Amino Acid (Theanine)-The amino acid theanine (5- N- ethylglutamine) constitutes more than 60 % of the total amino acid present in tea. This high theanine content is due to minimal fermentation. Theanine is responsible for tea's distinctive flavour, sweetness and relaxing effect. Other amino acids present include glutamine, asparagine, arginine and serine (14, 26, 27).

Caffeine is a psychoactive substance belonging to the methylxanthine group of alkaloids. The concentration of caffeine is higher in young tea leaves, ranging from 2 to 5 % (12). The caffeine content of an infused tea beverage is between 0 .01-0.02 %.

Vitamins – Green tea has a higher concentration of vitamins compared to other foods (9).

Vit B2 – Sencha, a variety of green tea, contains 1.4 mg of Vit B2 per 100 g.

Vit C – Acting as an antioxidant, Vitamin C helps prevent infections and cancer (9). Sencha contains the highest amount of vit C, which is crucial for collagen production. A deficiency in Vitamin C can impair collagen formation, weaken vascular walls and lead to scurvy (27).

Vit E – acts as an antioxidant and prevents the oxidation of lipids and fats within the body. Sencha is rich in Vit E (27).

Beta Carotenes – Beta carotene, the precursor of Vit A (Provit A), is absorbed through the intestinal walls and converted to Vit A in liver, which is essential for night vision. Matcha contains a large amount of beta carotene (27).

Vitamin U – is effective against gastric ulcers and is a main ingredient in gastrointestinal drugs. It is produced

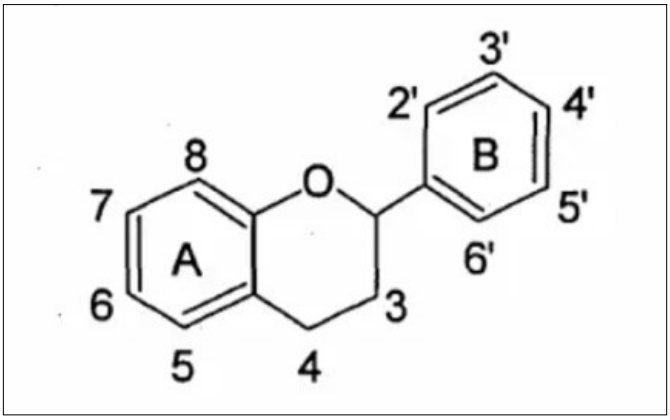

Fig. 3. Basic flavonoid structure (2-phenyl benzopyran).

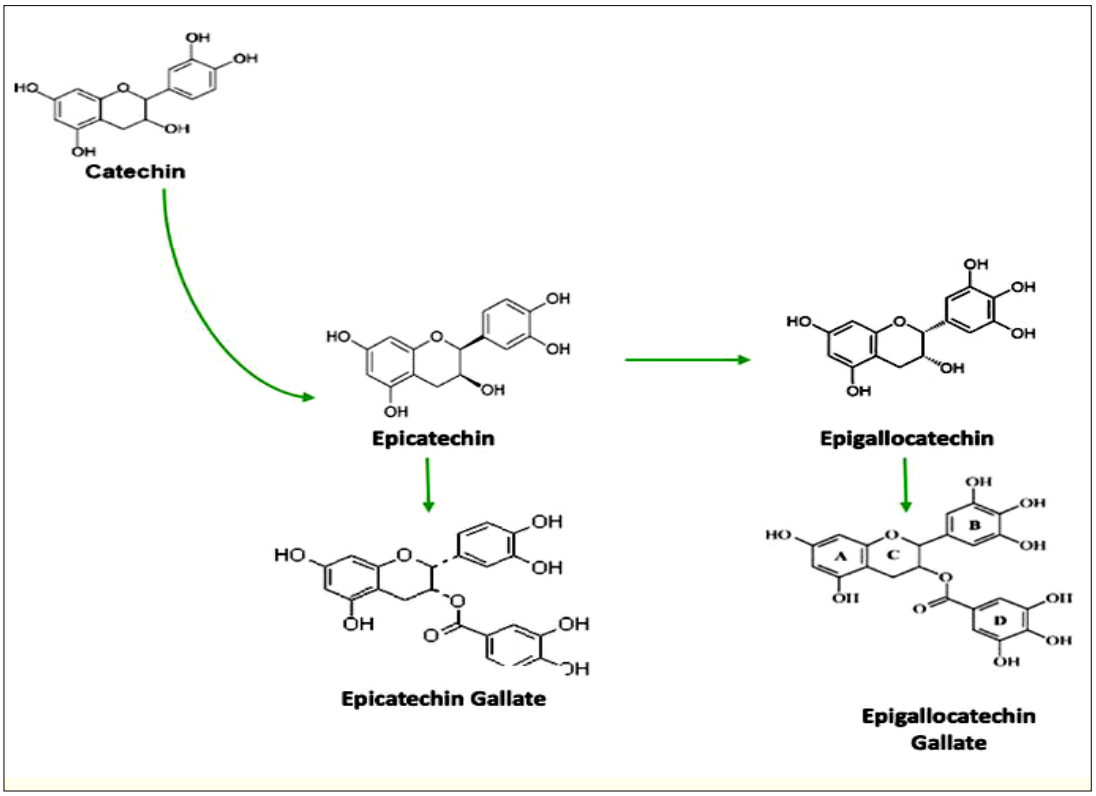

Fig. 4. Major catechins present in green tea.

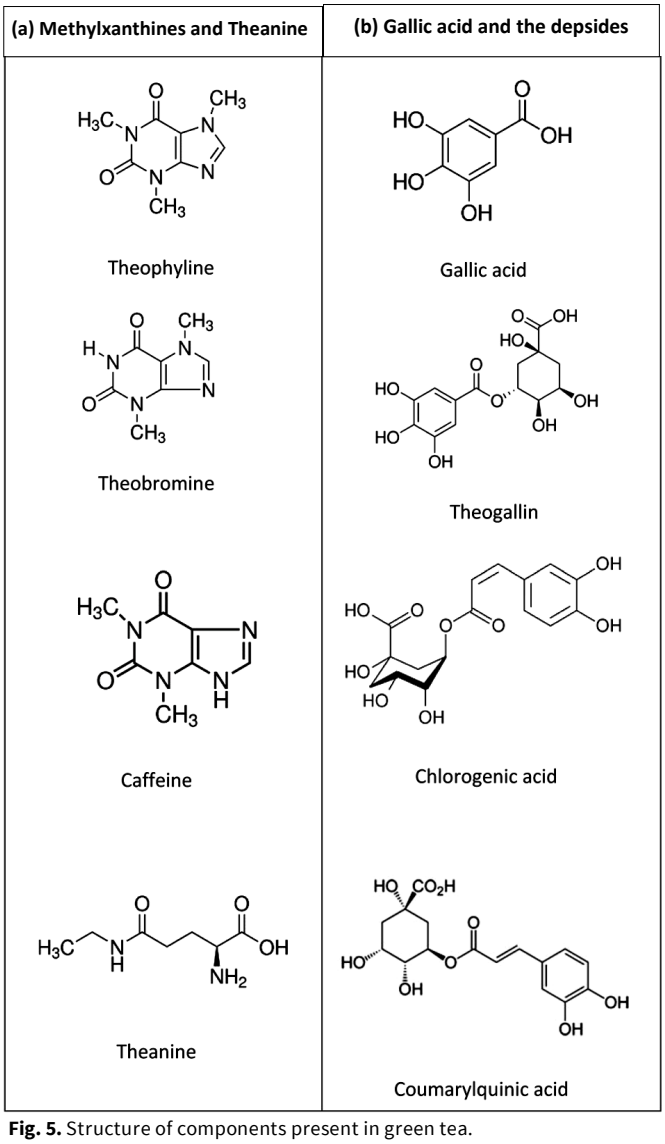

Fig. 5. Structure of components present in green tea.

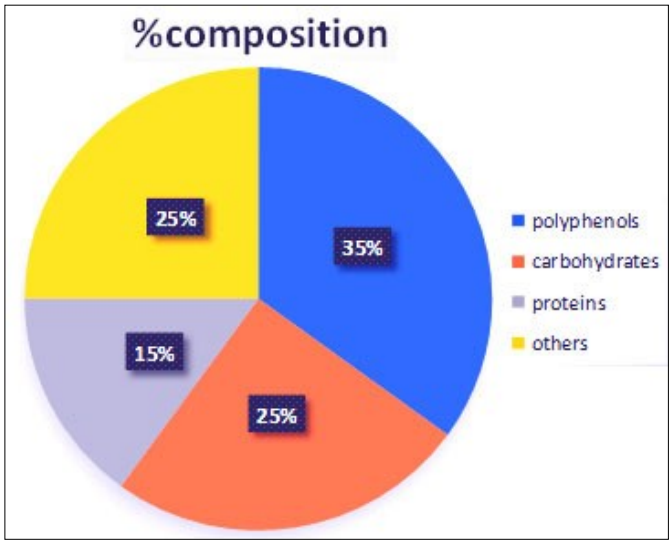

Fig. 6. Pie diagram showing percentage of each component in tea (11).

during the heating process of Gyokuro, Tencha and high-grade sencha. The unique "green laver aroma" of these teas is due to the release of vitamin U.

Folic acid – Matcha and Sencha teas contain large amount of folic acid.

Saponins – Tea leaves contain around 0.1 % saponins, which contribute to their astringency and bitterness. It is responsible for the frothing seen in teas like matcha (27).

Minerals – Dry leaves contain numerous elements such as fluoride, manganese and zinc. According to the data, 100 mL of tea provides 0.07 mg of Zinc, Magnesium and 5 mg of Calcium.

Fluorine – *Camellia Japonica* is the main source of fluorine, which is more abundant in mature leaves than in

younger ones. Rancha tea contains a significant amount of fluorine. The anticariogenic activity of fluorine is due to the formation of an acid-resistant layer on the tooth surface (27).

Minerals like potassium (K), Calcium (Ca), Phosphorus (P) and Magnesium (Mg) in amounts ranging from 5-7 %. It also contains small quantities of manganese (Mn) and Copper (Cu). Catechins in tea react with metal ions, aiding in the absorption of these ions (26). Manganese content in 100 mL of tea infusion is around 0.34 mg, according to nutritional value tables (12).

Oxalates – The concentration of oxalates in tea infusion depends on the brewing temperature. Oxalates react with minerals to form insoluble salts. Tea leaves contain 13 % polysaccharides and 3 % fats (16).

γ- aminobutyric acid (GABA) – Gabalong tea is prepared from raw leaves by drying in the absence of oxygen. The elements present in GABA help reduce blood pressure.

Chlorophyll – Teas grown in shaded areas, such as Gyokuro and Kabusecha, have higher levels of chlorophyll, which is necessary for photosynthesis. Chlorophyll has a deodorizing effect, which is utilised in chewing gums (27).

Fragrance components – Green tea contains around 200 fragrance components. The essence, or seiyu, which constitutes about 0.005 % of green tea, contributes to its fragrance. When raw tea leaves are heated, amino acids, saccharides and enzymes disperse, producing the tea's fragrance. The unique fragrance of fermented teas like oolong tea and black teas is released at high temperatures. The aroma of hot tea helps relieve stress and promote relaxation, making it useful for aromatherapy. Green tea also contains other flavor-rich compounds like terpenes, sesquiterpenes, oxygenated terpenes and organic acids (27).

Bioavailability

Bioavailability refers to the amount of a substance that can be detected in the blood, urine etc. after being introduced into the body. The highest concentrations of catechins appear in blood plasma between 1.5 to 2 h and in urine between 4 to 6 h after intake (2). The large molecular weight of EGCG (458 Da) constitutes to its low bioavailability (2, 18).

Metabolism of green tea

Catechins are metabolized in the liver, small intestine and colon, producing glucuronide and sulphate conjugates. They remain stable in solution within a pH range of 4-6 (5, 18, 28).

Bioactivities

Flavonoids extracted from green tea plant, are potent compounds that can stimulate the activity of certain enzymes and alter the functions of various cellular systems due to their antioxidant properties. Polyphenols are the main active ingredient responsible for the pharmacological effects of green tea, including scavenging free radicals and preventing and treating various infections, chronic sinusitis, cancer, diabetes and neurological problems (Table 2.)

Table 2. Health promoting properties of green tea (27).

Component	Functions
Catechins – Astringent in tea	Decreases Blood cholesterol
	Reduction of body fat
	Anticancer effect
	Antioxidant
	Anti-inflammatory
	Tooth decay prevention
	Antibacterial effect
	Anti-influenza effect
	Decreases high blood pressure
	Anti-hyperglycaemic effect
	Bad breadth –Deodorizing effect
	Biological system for synthesis of silver nanoparticles Bioactive coatings for implants(3, 5, 6, 12, 15, 16, 27)
Caffeine –Bitter component in tea	Stimulates central nervous system, improves alertness, prevents hangover
	Increases stamina
	Diuretic
	Cardiac stimulant (12, 27)
Theanine- flavour component	Nerve cell protection
	Causes relaxation
	Lowering of blood pressure
	Limits stimulant action of caffeine (5, 6, 16, 27)
Vitamin C	Protection of skin and mucosa
	Synthesis of collagen
	Antioxidant (27)
Vitamin B2	Protection of skin and mucosa
Folic acid	Prevention of foetal neural tube defects (NTD)
	Prevents atherosclerosis and improves circulation
Beta carotene	Improves night vision (27)
Vitamin E	Antioxidant
Saponins	Decreases blood pressure and prevents obesity, antiviral, antifungal
	antiallergic, anti- inflammatory
Fluorine	Prevents teeth caries
γ-aminobutyric acid (GABA	Decreases blood pressure
Minerals –Potassium, Calcium, Phosphorus, Manganese	Biological Regulators (12, 16, 27)
Chlorophyll	Deodorising effect (27)

Antioxidant activity

EGCG is the most biologically active substance in green tea, possessing the highest antioxidant potential. Antioxidants are a group of elements and compounds in our body that prevent or slow down cell damage caused by free radicals, which are produced in response to certain stimuli. Antioxidants protect the body against the invasion of germs and age- related diseases. Polyphenols prevents the production of free radicals, thereby reducing oxidative stress and cell death associated with many diseases (8, 16,

29, 30). The antioxidant activity of catechins results from their ability to chelate metal ions in redox reactions and neutralize free radicals (14, 24). The anticancer mechanism of green tea involves the induction of phase II antioxidant enzymes and inhibition of cell division (16, 29).

Anticancer potential

Flavonoids may act in the initial phase of primary cancer by enhancing the ability of target tissues to damage carcinogen. They prevent lipid peroxidation in the early stages by scavenging ions, which interrupts the radical chain reaction, thus preventing cytotoxicity and chromosomal damage (8). EGCG acts as an antitumor agent by inhibiting metalloproteinase activity (16, 29). It induces apoptosis by suppressing epithelial-mesenchymal transition and angiogenesis. Additionally, it exhibits anti-proliferation and anti -migration effects against cancer cells by down regulating the expression of STAT3, which plays a critical role in cell proliferation and metastasis (29). Catechins inhibit the release of tumour necrosis factor and suppress tumour growth (5, 12). EGCG is particularly effective against gastric cancer. Polyphenols can be applied topically as chemo preventive agent for skin cancer caused by ultraviolet radiation (30, 32). Catechins inhibit DNA methylation through DNA methyl transferases, which inhibit tumorigenesis (17). They also increase cellular energy expenditure in the mitochondria and inhibit the growth of tumor cells (2).

Cardiovascular disease

Polyphenols cause the expansion of coronary and brain vessels and lower blood pressure. They help prevent atherosclerosis and coronary artery disease by acting on signal transduction pathways in cardiovascular cells (5, 27, 29, 32). Flavonoids inhibit oxidation of LDL caused by free radicals, which leads to arteriosclerosis (8). EGCG effectively inhibit blood platelet aggregation and reduces the abnormal formation of blood clot, thereby reducing the risk of stroke (5, 32). Green tea prevents the oxidation of LDL cholesterol in the arteries, playing a significant role in preventing artherosclerosis (6). It also inhibits the action of thromboxane and the production of angiotensin-converting enzyme, which helps reduce blood pressure (6).

Antidiabetic activity

EGCG has been shown to increase the number and size of islets of Langerhans and the pancreatic endocrine gland. It reduces the detrimental effect of hyperglycaemia on cell viability and helps prevent diabetic retinopathy. Flavonoids can prevent pancreatic cell damage and activate insulin secretion. EGCG is effective in managing diabetes mellitus by reversing Klotho hypermethylation (29). It enhances renal functions down regulation TC, thereby reducing diabetic nephropathy. Flavonoids decreases blood sugar levels by inhibiting lipid peroxidation (8, 32). Green tea has been found to increase the sensitivity of insulin receptors and stimulate glucose-induced insulin secretion (2).

Neurodegenerative diseases

EGCG is effective against protein aggregation, iron accumulation, neuroinflammation, autophagy and neuronal cell death (29). Green tea can enhance working memory and is used in the management of neurological conditions such as dementia (29). High concentrations of colon- available green tea extract (CAGTE) counteract the damaging effects of beta-amyloid in Alzheimer's disease. Polyphenols improve normal brain function by inhibiting the activities of acetylcholinesterase and butyl cholinesterase (31). EGCG also has a protective effect on Parkinson's disease, reducing the ratio of CD3 and CD4 T cells in peripheral blood and serum and lowering proinflammatory cytokines. It protects dopaminergic neurons from degeneration and improves motor behaviour (29). Additionally, EGCG has been found to interact with the iron-export protein ferroprotein in substanstia nigris (29). Catechins are absorbed by the retina and other parts of the eye, making them effective against glaucoma (8).

Effect on fat metabolism

Caffeine and EGCG work synergistically to enhance the burning of adipose tissue and boost energy metabolism. Green tea inhibits the action of digestive enzymes and reduces the absorption of fat (2), leading to decreased body mass and weight loss. This makes it beneficial for preventing metabolic syndrome (12, 31). Additionally, tea consumption activates bile acid receptors, influencing bile metabolism (32, 33).

Against skin diseases

Polyphenols regulate biochemical changes associated with inflammation and cell proliferation. They inhibit carcinogens and modulate inflammatory markers induced by ultraviolet light. EGCG has been found to reactivate dying skin epidermis cells (5). A topical antiseptic ointment containing tea can be useful in treating impetigo (31). EGCG is used as an anti-aging agent and a therapeutic agent for FDP- induced skin aging.

Green tea is incorporated into antiseptic creams, mouth washes, facemasks to prevent infections, vacuum cleaner filters to reduce air borne microbial contamination (32).

Anti-cholesterol effect

Polyphenols help reduce total cholesterol levels, triglycerides, lipid peroxides, while increasing good cholesterol (HDL). They decrease the ratio of bad cholesterol (LDL) to HDL, thereby regulating lipid metabolism (5). Consumption of ground green tea reduces susceptibility of plasma and LDL to oxidation and modulates cholesterol metabolism (6). EGCG inhibits thrombin-induced aggregation and the proliferation and migration of smooth muscle cells (5, 27).

Osteogenic Property

Catechins influence bone remodelling by modulating various cell types, including osteoblasts, chondroblasts, adipocytes, myoblasts and stroma cells.

1. Polyphenols enhance bone mass and improve bone microstructure.
2. EGCG increases alkaline phosphatase activity and stimulates bone mineralization (28).

3. Polyphenol supports cell regeneration and protects against oxidative stress-induced cell differentiation and bone catabolism (30).
4. EGCG effectively modulated the expression of bone marker genes in mesenchymal cells, such as Run X2, Sp7 and osteocalcin. It also promotes the formation of mineralized nodules and inhibits osteoclast differentiation (34).
5. In human bone marrow mesenchymal stem cells, EGCG promotes osteogenic differentiation and has potential as an osteogenic agent in the treatment of osteoporosis.

EGCG can modulate bone morphogenic protein2 (BMP2), preventing collagen degradation and bone resorption by osteoclasts (31). It accelerates the mineralization of the bone matrix and enhances the expression of ALP and BSP genes. Increased ALP levels indicate osteoblastogenesis (34). Additionally, EGCG inhibits matrix metalloproteinase-9 (MMP-9), preventing osteoclast formation and strengthening the bone structure (30).

Anti- inflammatory effect

Increased production of IL-10, an anti-inflammatory cytokine, is responsible for the anti-inflammatory effect of EGCG. It is the key component that enhances the production of this cytokine. Polyphenols also improve microcirculation in affected areas and are effective against bacterial infection (6, 18, 31). Green tea inhibits the Cox-2 gene, which is associated with joint inflammation and arthritis (8). Studies have demonstrated that EGCG inhibits IL-Iβ induced inflammation and protects the chondrocytes (6).

Antimicrobial activity of green tea extracts

All 3 of these catechin derivatives, EGCG, EGC and EC-3-gallate contain an ester-linked galloyl moiety, which contributes to their significant antibacterial properties (23, 26, 35, 36). A nanocomposite combining green tea with nanoparticles has proven effective against oral microorganisms (36).

Antiviral effect

EGCG and ECG inhibit the synthesis of viral RNA in cells. They also block the enzyme neuraminidase, which is present on the surface of the influenza virus and have shown effectiveness against enterovirus, rotavirus and hepatitis (5).

Effect on HIV

EGCG exhibit a strong affinity for CD4 (+) T lymphocytes, binding to them and preventing the HIV virus from attaching to CD4 (+) lymphocyte. This action inhibits intracellular viral proliferation (5, 37, 38).

Antifungal activity

Catechin is pH – dependent. EGCG inhibits the growth of *Candida albicans* at low pH and has been found effective against yeast, chlamydia, filamentous fungi, mycoplasma and parasites (35, 39).

Anticariogenic activity of green tea

EGCG helps prevent dental caries by inhibiting the multiplication of *S mutans* and bacterial adhesion to enamel. It suppresses the activity of Glucosyl transferase and amylase, resulting in reduced acid production in dental plaque. Green tea extract is used as an antiplaque agent in antiseptic creams and mouthwashes (18, 23, 35).

Effect on Periodontal disease

Catechins deodorize halitosis-causing methyl mercaptan (40). At concentration of 250–500 g/mL, EGCG prevents the attachment and growth of *Porphyromonas gingivalis* on buccal epithelium (41). When delivered using a slow-release buccal system, catechins act against *Prevotella* and *P. gingivalis* species, thereby reducing gingivitis. EGCG also neutralizes toxic end products and virulent factors, such as collagenase, protein tyrosine phosphatase, alkaline phosphatase and gingipains, which are produced by periodontopathic bacteria that cause periodontitis (23, 41). For preventing dental caries and periodontal diseases, polyphenols are incorporated into dentifrices and mouthwashes (5).

Synergy of green tea with antimicrobials

Green tea catechins work synergistically with antimicrobial agents like penicillin against various oral microorganisms. This synergy is particularly effective against multidrug-resistant organisms, including gram-negative bacteria that produce extended-spectrum B lactamase (ESBL) and MRSA, methicillin-resistant *Staphylococcus aureus* (18, 42).

Antibacterial activity

Nearly a century ago, in 1906, Major MC Naught of the British Army Medical Corps hypothesized that tea possesses antibacterial properties (18, 23). This antimicrobial activity is attributed to the production of reactive oxygen species generated from EGCG. Studies have shown that EGCG has significant immunomodulatory effects (43). Purified EGCG compounds have demonstrated strong bactericidal and inhibitory effects against a range of pathogenic bacteria (Table 3).

Side effects and risk of green tea

While catechins offer numerous health benefits, high doses can lead to complications due to caffeine content, aluminum presence and iron bioavailability issues. For patients with renal failure, aluminum accumulation can result in neurological problems. In cardiac patients and pregnant women, the caffeine content may alter cardiac rhythm (26). Excessive EGCG intake can cause stress-induced cellular damage due to increased radical production (5, 26). There have been rare reports of liver problems, including acute liver cytotoxicity, following the consumption of high concentrations of green tea extract (2, 26). High concentrations of tea can negatively affect iron bioavailability because tannins and polyphenols bind non-heme iron, potentially leading to iron deficiency anemia (12). Additionally, high doses of green tea have been linked to thyroid enlargement in rats (26). Oxalates in tea can react with minerals to form insoluble salts, potentially causing nephrolithiasis (12). Caffeine may lead to sensitivi-

Table 3. Four mechanisms of action of catechins against microorganisms.

Inhibiting cell wall synthesis	a. The catechins bind to lipid bilayer cell membrane of bacteria and produces H_2O_2 which causes increased
	b. Bacterial biofilm formation is inhibited by damaging
	c. Transmembrane transporter proteins which is in charge of secretions of toxins is ineffective because of cell membrane damage (18)
	d. The LPS lipopolysaccharide present in the outer membrane of gram-negative bacteria is negatively charged thus it prevents catechins from binding on
Inhibition of fatty acid synthesis	a. The specific enzymes reductases (Fabg, FabI) involved in type II fatty acid synthesis are inhibited by EGCG (18, 47, 48)
	b. It also inhibits bacterial production of toxic metabo-
Inhibition on other bacterial enzyme activity	a. Catechins inhibits enzymes like protein tyrosine phosphatase and cysteine proteinases
	b. It interferes with bacterial DNA replication by inhibiting DNA gyrase (42)
	c. The ability of the microorganisms to synthesize folate is prevented by inhibiting the enzyme dihydrofolate
	d. The ability of microorganisms to synthesis adequate energy is blocked by inhibiting the activity of bacterial ATP synthase (18)
Inhibition of other bacterial enzyme functions	a. Prevents methicillin-resistant *Staphylococcus aureus* (MRSA) from synthesizing PNP2 which causes resistance
	b. Prevents conjugative transfer of R plasmid and activity of efflux pumps and act against *Escherichia coli*
	c. Catechins prevents *Helicobacter pylori* from attaching to the gastric epithelial cells' Toll-like receptor-4 (TLR -4) and guards against gastric diseases (49-51)

ty issues such as insomnia, irritability, stomach upset and dyspepsia. When combined with other stimulants, it can elevate heart rate and blood pressure. Excessive green tea consumption can lower serum potassium levels, leading to hypokalemia and muscle weakness. Polyphenols can disrupt renal function and green tea may also inhibit the metabolism of warfarin (52).

The primary side effects of catechins include gastrointestinal distress and central nervous system stimulation. Hepatotoxicity has been reported with green tea supplements or beverages (53). Green tea ointments may cause allergic reactions, leading to cervical and vaginal inflammation as well as vulvar burning (54). An additional drawback of catechins is the unpleasant taste of solutions used as mouthwashes (18). Excessive consumption of tea can be toxic due to reactive oxygen species that may damage DNA. Furthermore, tea can become contaminated with heavy metals like lead and aluminum, potentially causing additional side effects (55, 56).

Recommended dosage and precaution

The recommended dosage of green tea is 250-500 mg per day, typically obtained from drinking 3-5 cups or about 1.2 L. Consuming 3-5 cups of green tea daily is generally considered safe for most people. For optimal antioxidant levels and stress reduction, it is best to drink a cup of green tea in the morning, 1-2 h after breakfast, or in the afternoon, 1-2 h after lunch (57).

For cardiovascular patients, a minimal dose of 5 cups of green tea per day is recommended. Patients who consumed 4 or more cups of tea daily showed a reduced risk of stroke. However, individuals with severe liver problems should avoid green tea. Due to its relatively low caffeine content, green tea can be used by diabetic patients, but only in minimal doses (57).

The risk of lung cancer is reduced in patients who consume 1 cup of green tea per day. Women who drink 3-4 cups of green tea daily show a reduced risk of rheumatoid arthritis. Additionally, individuals who drink 2 cups of green tea per day have a lower risk of Parkinson's disease (58). For diabetes patients, a dosage of EGCG ranging from 84-386 mg per day is effective in supporting glucose homeostasis. However, caffeine-rich drinks may raise blood sugar levels in individuals with type 2 diabetes. In terms of obesity, a green tea extract tablet containing 125 mg of catechins or a daily green tea beverage with 625 mg of catechins can be beneficial for overweight and obese adults. Consuming 240 mL of green tea daily can be advantageous for managing metabolic syndrome.

For depression, drinking 2-4 cups of green tea daily has been associated with a lower prevalence of depressive symptoms. During pregnancy, due to its caffeine content, green tea should be limited to no more than 600 mg per day. Daily consumption of green tea has been shown to reduce the risk of chronic obstructive pulmonary disease (COPD). Drinking 3 cups of green tea (720 mg) contributes to the absorption of 4 mg of fluoride and helps combat oral bacteria. It is advisable not to consume green tea on an empty stomach due to the potential for hepatotoxicity from excessive EGCG levels (59).

The addition of milk to tea can have 2 distinct effects on its antioxidant content. Milk reduces the ABTS* radical scavenging capacity of green tea (an electron transfer-based assay) by 60 %. Conversely, it increases the chain-breaking antioxidant capacity of tea in lipid peroxidation assays by 19 %. Reheating tea is generally safe, but since it contains caffeine, it becomes more concentrated during the process. Reheating tea that has been left for more than 4-8 h is not advised, as it can lead to adverse effects such as irritability and sleep disturbances. Reheating may also cause the breakdown of certain compounds and changes in pH levels, which can contribute to increased acidity. Additionally, reheated tea might lose its flavor and nutritional qualities. If tea is left for a prolonged period and then reheated, bacteria may begin to grow, leading to unpleasant taste and food poisoning symptoms like nausea and vomiting. The bioavailability of active compounds in tea appears to be unaffected by the addition of milk, although milk may accelerate bacterial growth. This can result in an unpleasant taste and potential food poisoning symptoms (60).

Conclusion

Green tea is a crucial herb in biomedicine due to its extensive use in pharmacology. Numerous studies have demonstrated the pharmacological activities of its chemical components. EGCG, the most biologically active catechin in green tea, contributes significantly to its health benefits. The high phenolic content of green tea imparts various pharmacological effects, including antioxidant, anti-inflammatory, antimicrobial, anti-cancer, anti-diabetic, anti-cholesterol, neuroprotective properties and benefits in treating metabolic disorders.

Recent advancements in nanotechnology have explored the use of green tea in lipid nanocapsules and liposome encapsulation to deliver EGCG. This approach shows promise for treating chronic diseases. Research is also focusing on targeted drug delivery by combining green tea catechins with nanoparticles. Developing biomarkers to determine green tea consumption and molecular markers for its biological effects will enhance our understanding of safe dosing for optimal health benefits. Herbal medicines, being complex combinations of various compounds, act synergistically to provide diverse benefits. The application of green tea extract with nanoparticles against systemic conditions is showing encouraging results as a therapeutic agent. Given the potential limitations of modern medicine, the antimicrobial effects of medicinal plants and their extracts are receiving increasing attention.

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