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# A Review of the Health Benefits of Tea: Implications of the Biochemical Properties of the Bioactive Constituents

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**Abstract**

Tea is the second-most drank and refreshing beverage after water since the time immemorial. Tea harbours more than 700 bioactive compounds viz, different classes of polyphenols, unique amino acid L-Theanine, alkaloids (Caffeine, Theobromine), and Volatile Flavor Compounds (VFC). Tea's polyphenols make its inherent therapeutic potential unlimited. Tea's significance in managing cancer, diabetes, stomach ulcer, influenza, neurological diseases, etc. is well-documented. However, advantageous biochemical capabilities of tea have yet to be fully utilised. Hence, this review aims at to examine tea's variety, drinking habits, biochemistry, and therapeutic qualities. A number of significant online resources, including Google Scholar, Pub Med, Science Direct, and others, were searched for various research works on tea and its health-promoting qualities by using keywords like tea, health benefits, bioactive components against diseases, etc. Current review highlighted that drinking a cup or more green tea is recommended for improving antioxidant status and to manage diabetes and obesity related problem. However after detailed review work on tea it become clear that not only green tea but also other varies of tea like black, white tea are also harbour lots of bioactive molecules since they are processed from same plant. Tea improves antioxidant status and manages diabetes and obesity. It also helps prevent and cure heart disease, malignancy, digestive dysfunction, and metabolic disorders including obesity and diabetes. Epigallocatechin Gallate (EGCG), found in tea, has been shown to reduce complications from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV 2) infection. When taken in its traditional form to manage ailments, tea is sometimes controversial

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due to a lack of confirming evidence of its benefits. The paper covers the numerous health advantages of tea, focusing on the specific components contributing to such benefits, and stresses the value of diverse brewing processes.

## Introduction

Since ancient times, the human population has sought health-promoting and relief providing substances from nature. The medicinal herbs and plants used to prevent and cure diseases and infections have been known and documented by mankind since times immemorial. This age-old practice of using plant materials that are rich sources of phytonutrients and neutraceuticals as therapeutic agents for alleviating a wide variety of human ailments has gained immense popularity.[1]

India has been globally recognized as the treasure house of medicinal plants, herbs, and spices. Basic materials are derived from different plant parts, including leaf, berry, modified stem, bud, rhizome, latex, seed, bark, root, stigma, flower, etc., which have primarily been used in cooking to enhance the flavour of food and to excite taste buds. However, the so-called culinary herbs and spices have, over time, swiftly made their way from the kitchen to the clinic, owing to their special health-promoting activities. Their wide range of physiological and pharmacological characteristics has enabled this. They have made significant contributions to the nutritional value of dietary plans by adding antioxidant-rich phytochemicals without compromising the food flavour. They have also been studied to exhibit medicinal properties and preventive effects against diseases and infections, aiding overall health and well-being.[2,3] This comprehensive review article summarizes the roles of tea derived bioactive constituents as human health beneficial role, which generally enhances the bioavailability of the tea constituents.[4]

Tea is a commodity that is manufactured from the leaves, leaf buds, and internodes of numerous cultivars and sub-varieties of the *Camellia sinensis* plant. This plant is widely farmed in the humid tropical climate of Southeast Asia, and it provides a wide range of tastes and fragrances. It is a beverage with a soothing aroma and refreshing taste. It is the second most preferred beverage next to water, with an average per head consumption of around 450–500 ml per day, consumed by approximately two-thirds of the world's population.[5] Different consumers have different preferences for tea based on the degree of fermentation, taste, and color.[6] Tea is primarily drunk for the stimulus and comforting warmth. However, various medicinal attributes of tea are also known to us. Tea is considered a rejuvenator and often acts as a therapeutic adjuvant for several aliments for people from all walks of life.[7]

Several countries like China, India, Sri Lanka, Kenya, Japan, Vietnam, Indonesia, and Turkey produce tea. India is the second-largest tea producer globally, where Darjeeling and Assam in the North-East contribute to a significant portion of the national produce. Other than that, tea is also grown in some parts of South India. Darjeeling black tea is mainly preferred for its incomparable qualities of rare fragrance, while Assam tea is famous for its color.

## Types of Tea Available in the Market

Tea (*Camellia sinensis*) in Figure 1 is a well-known evergreen shrub of the Theaceae family. Generally, two different tea plant varieties are available: *Camellia sinensis* var. sinensis and *Camellia sinensis* var. assamica (Integrated Taxonomic Information System, 2022).

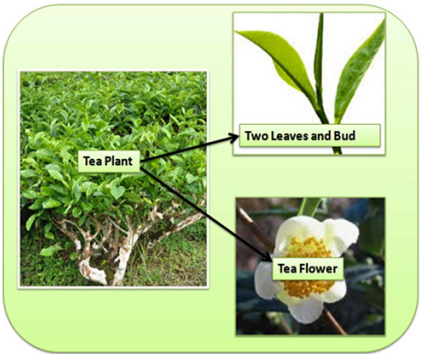


**Fig.1: Different parts of a tea plant *Camellia sinensis***

After plucking, the tea leaves are processed to make different types of tea based on market demand. As a result, tea is available in various types, of which four types are the most common. white tea[8] green tea[9] oolong tea[10] and black tea.[11] The classifications of these teas depend on the preparation and processing of tea leaves. The tea processing has five basic steps—plucking, withering, rolling, oxidizing, and drying.

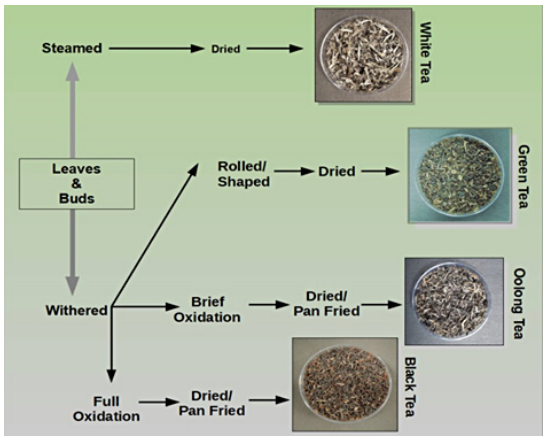


**Fig. 2: Processing regimes for White, Green, Oolong and Black Tea**


**Fig. 3: Different types of tea brews**

The primary difference among these teas is their degree of fermentation (i.e., enzymatic oxidation of tea leaves). Besides, they can also be distinguished by the season of picking (flushes), positions, and many other factors. There are four main steps of processing tea leaves after plucking,[12] which are shown in Figure 2. From the perspective of tea manufacturing, fermentation refers to the enzymatic oxidation (polyphenol oxidase) of tea leaves by allowing them to dry. The degree of fermentation results in many significant changes in the biochemical content of the leaf[13] as well as the colour of the brew, as seen in Figure 3.

Green tea, white tea, oolong tea, and black tea are produced from the steeping of differentially produced tea leaves obtained from the same tea plant (*Camellia sinensis*).

**Biochemical Composition of Tea Leaves**

Polyphenols collectively represent a group of approximately 500 phytochemicals, which occur as micronutrients in plants. In a nutshell, polyphenols are phenolic structures associated with different organic acids and carbohydrates. Due to their association with sugars in plants, they can be present in the form of glycosides. The complexity of polyphenols ranges from pure phenolic acids to highly complex condensed tannins; it is a generic term where multiple phenol groups are attached to a chemical substance. Tea also contains diversified polyphenols.[14] Much scientific research has proved that secondary tea metabolites have anti-diabetic,[15] cardio-protective,[16] anticancer[17] antimicrobial,[18] and antiviral properties.[19]

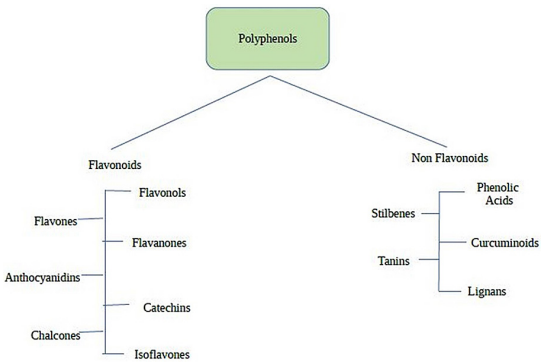


**Fig. 4: Flowchart ofdetailed classifications of polyphenols**

Flavonoids are secondary metabolites present in the drink. They are not known for participating in plant development and growth. However, they are the largest group among all the polyphenols by weight (approx.30% [w/w]). There are seven main classes of flavonoids: flavones, flavonols, flavanones, flavanonols, flavanols (catechins), chalcones, and

anthocyanins. Amongst them, flavanols (catechins) and flavonols (quercetins) are the two main groups.[20] Catechins are the major groups of flavanols. Fresh tea leaves catechins are monomeric.[21]Green tea catechins range from 20%–30%,[22] while black tea catechins range from 3%–10%[23] of total dry weight.

Tea is loved by people worldwide for its astringency, color, and aroma.[20] Due to these astringency characteristics, it acts as a defense system for plants against harmful insects. Further subdivided into derivatives based on the -OH group, Catechins are EC, ECG, GC, EGC, EGCG, and GCG,[24] as shown in Figure 5. Published in Henning *et al.* (2013), per cup of green tea contains 90–100 mg of EGCG. Besides catechins, the three most essential flavonols in tea are quercetin, kaempferol, and myricetin, as described by Wang *et al.* (2000), shown in Figure 5 A. Balentine *et al.* (1997) stated that the aqueous extract of tea consists of 2%–3% of flavonols.

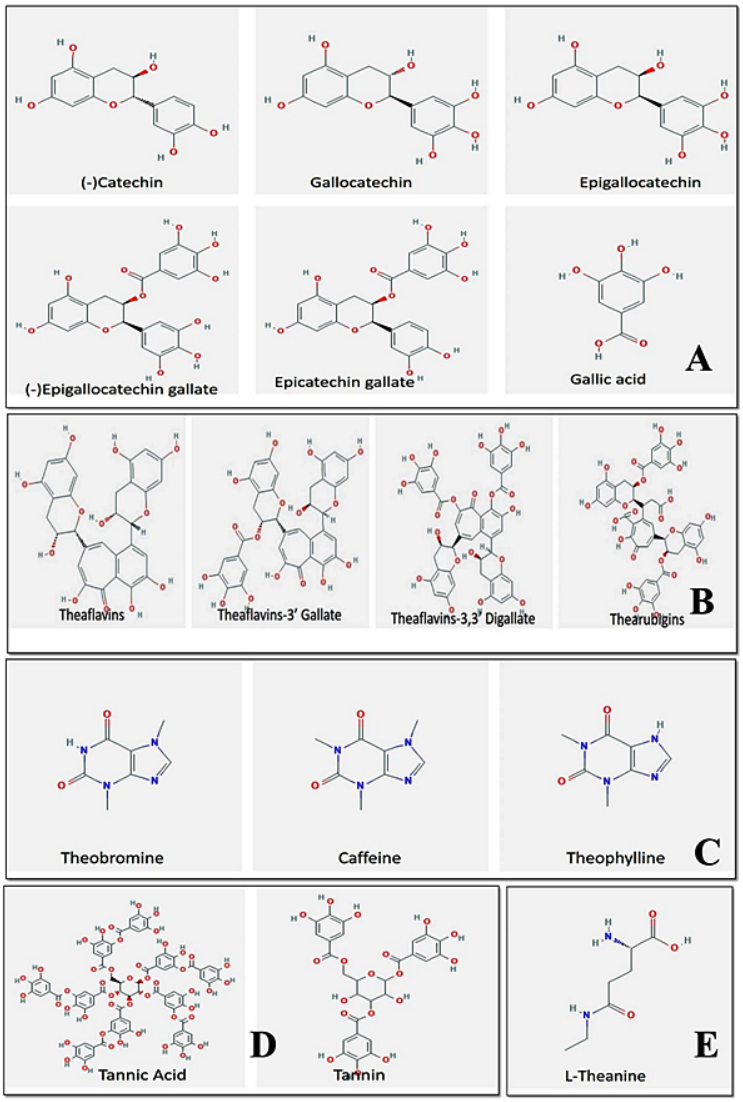


**Fig. 5: A. The image representing the chemical structure of flavanols; B. The image representing black tea polyphenols; C. The biochemical structure of methylxanthines; D. The biochemical structure of tannic acid and tannin; E. The biochemical structure of L-Theanine**

In addition, oxidation of tea leaves leads monomeric catechins to form complex compounds like theaflavins and thearubigins. Out of these, thearubigins are the most abundant black tea pigments; an estimated 60% are present.[25] The distinct red-brown coloration of black tea is due to these two essential polyphenolics. Theaflavins are generally present as theaflavins 3' gallate and theaflavins 3,3' di gallate (Figure 5B)

Another less abundant polyphenolic compound is theasinensins (dimeric flavan-3-ols), a colorless substance thought to be present in tea that is intermediatory to theaflavins and thearubigins. As a result, it is mainly present in oolong tea.[26] Other than these, some substances are present in tea, such as saponins, chlorophylls, carotenoids, alkaloids, caffeine, theobromine, and theophylline (Figure 5C). An average tea infusion contains around 50mg to 90mg of caffeine.[27]

Moreover, tea contains tannin and tannic acid in addition to the compounds (Figure 5D). Though some research articles highlighted their significant bioactivities, they are found to be toxic when taken in excess and may be attributed to gastric cancer.

Recently, black, as well as other types of tea, are believed to provide relaxation. The substance responsible for a sense of peace is a unique bioactive amino acid, “L-Theanine” (Figure 5E). It constitutes 1% to 2% of the total dry weight of tea leaves and about 50% of the total free amino acids.

**Tea and Healthcare**

Natural products are chemical compounds formed from living organisms available in nature, such as bacteriophages and plants, which have laid the beginning of many enduring medical treatments over the decades. The most popular, well-known products are morphine (opioid analgesic), isolated from the poppy plant (Papaverrhoeas). Another example is quinine (antimalarial drug) isolated from the bark of Cinchona (Cinchona succirubra).[28] Worldwide, 60% of drugs used in cancer treatment are directly from natural products.[29] Recently, pharmaceutical companies have stopped investing in natural products because of the new type of synthetic approach, which is less time-consuming and inexpensive.[30] In general, natural products are chemically different in their compositions from synthetic drugs[31] because of the complex biosynthetic pathways they are isolated with. These pathways are more efficient than synthetic routes. They are challenging to imitate because of complex chemistry and relevant evidence, leading to disadvantages for drug companies trying to purify the hit compound. The crude extract of the natural product was clinically valuable and could be produced on a large scale. In Asia, *Camellia sinensis* is a plant that is accepted as a good source of health-promoting factors and leaves infused in water; it is used by millions of people worldwide.[32]

Tea has been the most preferred beverage globally since its discovery. Tea is famous worldwide because it is pleasuring, socially acceptable, inexpensive, and safe. On the other hand, people gradually realized that tea could not only be consumed as a beverage but could also be used as a natural source of medicinal substances as well. Since its discovery, it has been used as a natural antimicrobial agent in ancient China. With time, the whole world came to know its immense antioxidant and anticancer properties. Gradually, several disease prevention capacities were observed by all the people of the world. The biochemical analysis of tea revealed that it contains more than 700 bioactive components, which are responsible for its therapeutic activities. Among the several bioactive components, the most essential and unique biochemicals are catechin and its derivatives, viz. GC, EGC, EGCG, EC, ECG, caffeine, tannin, and L-Theanine. The use of tea can help prevent some types of cancer, cardiovascular disease, diabetes, kidney stones, bacterial infections, dental cavities, neuro degenerative diseases, and some viral infections.[33]

**Alzheimer's Disease**

Alzheimer's disease (AD), or simply Alzheimer's, is a chronic neurodegenerative disease that is the most common form of dementia. The onset of the disease is generally marked with symptoms of short-term memory loss, which advances as the disease progresses. Later symptoms may include problems associated with language and speech, disorientation which provides to getting lost easily, mood swings, lack of motivation, little self-care, behavioral issues, etc. As the patient's condition deteriorates,

symptoms of withdrawal from family and society are also noticed. Gradually, body functions crucial to survival are lost, ultimately leading to death.

It has been suggested that tea possesses potent antioxidant properties. They are rich in phytochemicals, including flavonoids, tannins, caffeine, polyphenols, behenic acid, theophylline, theobromine, anthocyanin, gallic acid, and finally, EGCG, which is potentially considered to be the most active ingredient. Flavonoid phytochemicals, known as catechins, within tea offer several benefits for reducing the risk of AD by targeting the various common risk factors, including hypertension, cardiovascular disease, and stroke. Studies have also proved that catechins may play an essential role in the prevention of the formation of amyloid-β plaques and, thereby, enhance cognitive functions and, thus, may be helpful in the treatment of patients who are victims of AD. Furthermore, other phytochemicals found within tea offer a variety of critical antioxidant properties as well.[34]

Green tea polyphenols are broadly classified into four different categories based on their structural variations in hydroxyl groups present: EGCG, EC, EGC, and ECG. Much scientific evidence suggests that drinking green tea may reduce the likelihood of developing Alzheimer's disease (AD), Parkinson's disease (PD), or cognitive dysfunction in dementia.[35]

As compared to Vitamin C and E, EGCG has shown more effective as radical scavenging because they contain three hydroxyl groups in the B ring and galloyl moiety with three hydroxyl groups in the C ring.[36, 37]

High polyphenol content in tea contributes to its beneficial effects. Polyphenols present in green tea showed radio-protectant activity, such as the prevention of neurotoxin-induced cell injury.[35] In spite of there being no epidemiological evidence in human studies of the benefit of green tea for AD, several studies in animal and cell culture models have established that EGCG from green tea may affect several potential targets associated with the progression of AD.

EGCG protects against neurotoxicity induced by beta-amyloid in cultured hippocampal neurons, an effect that is attributed to its antioxidant properties.[38] EGCG also regulates APP processing by activating PKC to the non-amyloidogenic soluble APP (sAPP), thus preventing neurotoxic beta-amyloid formation.[39] EGCG and other green tea catechins have also been shown to inhibit the beta-secretase enzyme (BACE1) that is responsible for processing sAPPto beta-amyloid, thus having a potentially synergistic inhibitory effect on the production of beta-amyloid.[40]

The present therapeutic approaches for AD are merely intended for the treatment of symptoms and offer only partial benefit without possessing any disease-modifying activity. Novel promising advancements propose the usage of naturally occurring plant flavonoids to revert the progress of the disease. Recent human epidemiological and animal data suggest that tea drinking may decrease the incidence of AD.[41] Various studies were carried out to determine whether or not the treatment of transgenic (Tg) mice with green tea catechin (GTC), a radical scavenger, improves AD phenotypes.[42] However, more recent studies show that the radical scavenger property of green tea polyphenols is less likely to be the sole clarification for their neuro protective ability and, as a matter of fact, a broad spectrum of cell signaling events may be well responsible for their biological actions. Studies on the effects of green tea polyphenol (GTP) on the behavior of AD-like mice induced by D-galactose and Abeta25-35 have also been carried out. GTP amended the deleterious effects of D-galactose and Abeta25-35 and, thus, improved the mouse's learning and memory and reduced the error numbers significantly. At the same time, the autonomic activities of the animal observed a significant increase.[43]

Brain aging and various neuro degenerative diseases of the elderly, such as Alzheimer's itself, are characterized by damage due to oxidation, homeostasis impairment of redox metals, and inflammation. Polyphenols present in tea can counteract these alterations in vitro and are therefore touted to possess potential anti-aging and brain-protective properties, as also indicated by several studies.[44]

The intake of black tea extract (BTE) reduces memory loss and learning deficits in Alzheimer's rats. The BTE also attenuates the improved activity

of acetylcholine esterase (AChE), which is induced by aluminium chloride.[45]

Catechin flavonoids are present in GTE and are defined as the active components of green tea and also account for their therapeutic properties. The ester formed by epigallocatechin and gallic acid, (−)-Epigallocatechin-3-Gallate [EGCG; (2R,3R)-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-3,4-dihydro-2H-1-benzopyran-3-Cyl 3,4,5-trihydroxybenzoate] represents the primary bioactive polyphenol present in the solid GTE (which possesses a 65% catechincontent). Several studies have indicated that EGCG also has several important anti-atherogenic and anti-inflammatory properties,[46] with an array of neuro-protective effects against various cerebrovascular diseases.

Most of the drug therapies that are carried out for Alzheimer's are based on the cholinergic hypothesis, which prompts that a deficiency in the production of the neuro transmitter acetylcholine marks the beginning of AD. Some polyphenolics of green tea, which are reported as AChE and BChE inhibitors, are used in the treatment of AD. The results obtained from molecular docking revealed that polyphenols exhibit interactions and inhibit by binding with A ChE and B ChE.[47]

The various forms of tea, mainly black and green, possess an array of chemicals that are of prime importance in the treatment of AD and retarding its progression in an individual. Polyphenols and catechins are the two main constituents responsible for arresting the advancement of the disease. They prove their importance in the diet and de-mark tea as a source of a possible cure for AD.

**Diabetes**

Diabetes mellitus [DM] (commonly known as diabetes) results in high sugar levels in the blood and is linked with polyuria, polydipsia, and polyphagia. DM type 1 is characterized by hyperglycemia and insulin resistance, whereas DM type 2 is linked with the failure of cells to respond to insulin. The latter is the most common form and is responsible for (90–95) % of DM cases.[48]

Green tea polyphenols (GTP) have been found to increase glucose tolerance levels ($P<0.005$) at 60 minutes in rats and to reduce serum glucose level in alloxan diabetic rats.[49] The decrease in glycemia by 30% of control post 2 hours of glucose loading after providing an aqueous extract of *Camellia sinensis* (450mg/kg) has been noted by Shokrzadeh *et al.* (2006). Improved insulin resistance has been linked with glucose transport IV's high level of expression in the fructose-fed rate.

The risk of type 2 diabetes can be curbed by control of postprandial hyperglycemia via green tea, which also promotes glucose metabolism in humans at 1.5 gm/body in OGTT.[50] Post 12 weeks of green tea supplementation (0.5gm of lyophilized green tea powder dissolved in 100ml of deionized distilled water), lower fasting levels of glucose, insulin, triglyceride, and fatty acid have been noted. GTP has also been linked with an increase in basal and insulin-stimulated glucose uptake of adipocytes.[51]

GTP having galloyl residues inhibits the transport activity of sodium-dependent glucose transporter performing intestinal glucose uptake (SLGTI) competitively (Yoko *et al.*, 2000). Green tea has been found to have the highest hydrogen peroxidase inhibition value (65.50%) at 250 µl/ml concentration.[52]

Tannins (components of tea) are involved in the enhancement of glucose uptake and inhibition of adipogenesis.[53] Consumption of 16–30 cups of green and oolong tea per week has been linked with low ratios of impaired fasting glucose (IFT) or impaired glucose tolerance (IGT). Post soaking with tea catechin (which acts as an elicitor), the total soluble phenolic content of barley and wheat increased, and their anti-diabetic activity was determined.[54] Tea phytochemicals like polyphenols, methylxanthines (mainly caffeine), and L-theanine contribute to the anti-diabetic, neuroprotective properties and antioxidant potential of tea, thus having positive effects on DM related problems and protecting the brain against oxidative damage (since DM is linked with neuro degenerative diseases).

Meal planning for type 2 DM patients can be facilitated by the antioxidant activities and phenolic compounds of tea, which also contribute to maintaining plasma antioxidant levels since vascular diseases linked to type 2 DM can be

prevented by the antioxidants present in plants.[52] Further, it can be noted that hyperglycemia-induced pathogenesis can be reduced by the phenolic antioxidant-rich dietary strategy.[55]

Black tea water extract has the highest α-glucosidase inhibitory activity, with white and oolong tea following in second and third. It was also found that tea extract can inhibit the alpha-glucosidase and alpha-amylase activity that providing a biochemical rationale to control glucose absorption by dietary management of type 2 DM and for future in-vivo studies.

In a streptozotocin-induced diabetes model of rats fed with 0.5% aqueous extract of white tea for four weeks, a reduction in blood glucose concentration and increase in glucose tolerance was noted to contribute to the fact that white tea can reduce diabetes-associated abnormalities.[56] Green tea and black tea extracts were fed to a diabetic mouse model with a low dose streptozotocin and a high-fat diet, which resulted in low blood glucose levels; green tea is more effective in anti-hyperglycemic activity. It has also been found that green tea showed an anti-diabetic effect through insulin resistance, whereas black tea showed the same through insulin secretion.[57] Tea has a natural insulin-enhancing activity that is decreased by using creamers and soy milk, and the predominant active component is epigallocatechin-3- gallate.[58]

Polyphenols and iso flavones, components of tea, because of their strong radical scavenging and antioxidant effects, contribute to the prevention of diabetes. Caffeine, one of the critical components of tea, decreases insulin sensitivity by increasing the concentration of serum epinephrine but also lowers the risk of type 2 DM. Additionally, oolong tea, along with anti-hyperglycemic agents, was found more beneficial in lowering plasma glucose than the drugs alone.[59]

In Singapore, considering the case of Asian men and women, daily intake of black tea and coffee and not green tea is linked with low risks of type 2 DM. An inverse relation has been identified between regular black tea and coffee drinkers with a risk of DM type 2.[60]

Saponin, a component of tea, is found to have anti-diabetic activity. It has the ability to reduce plasma blood glucose level (hypoglycaemic activity); remain unavailable to glucose autoxidation, be a good chelator of metals; enhance antioxidant activity, prevent reactive oxygen species (ROS) formation in diabetes; modulate the expression of many genes associated with lipid metabolism, thus regulating hyperlipidemia associated with diabetes and suppressing the appetite signals in the hypothalamus, leading to reduced food intake and body weight gain since obesity is linked with diabetes. Thus, saponins can be considered excellent for the treatment of diabetes in comparison to anti-diabetic drugs, which have side effects like weight gain.[61]

L-theanine is a naturally occurring bioactive amino acid found in tea. It is an insulinotropic agent that also provides partial protection to pancreatic cells under oxidative stress. Diseases can be controlled or managed using L-theanine.[62]

In another study, it was revealed that black tea might have an essential role in lowering surrogate markers of insulin resistance, and long-term tea drinking may modify fasting glucose/insulin levels, slowing diabetes progression.[63]

As a result of the preceding research, it is reasonable to conclude that tea brew is an important natural therapy in DM.

**Cancer**

Cancer is a disease in which abnormality of cellular growth is observed. Cancer cells proliferate uncontrollably, leading to the formation of tumors. Regardless of the elaborate research and rapid development in cancer therapy and treatment, it remains to be a deadly disease posing an immense health risk to people across the globe. However, evidence points out that cancer can possibly be prevented by changing lifestyle transformations such as no smoking, moderate alcohol consumption, low-calorie food intake, healthy workout, exercise, and increased intake of whole grains, fruits, and vegetables.[64] Studies suggest that green tea exhibits bioactivity in antioxidation, angiogenesis, and anti-proliferative assays, which play a significant role in the prevention and treatment of various types of cancers.[65,66]

EGCG, which is the most powerful bioactive anticancer polyphenolic component present in tea, inhibits multiple cell signaling pathways that are responsible for cancer development, including activator protein 1 (AP-1) NF-κB, nuclear factor of activated T-cells (NFAT) and β-catenin (1–5).[67] It has also been reported that EGCG is capable of inhibiting DNA methyl transferase (DNMT) activity and once again reactivating those genes in cancer cells where methylation was silenced, suggesting the potential use of EGCG – a commonly consumed dietary component for the prevention of cancer.[68]

Chemoprevention of cancer is defined as the use of natural or artificial substances to prevent or repress the initiation, advancement, spread, and metastasis of cancer. It has been studied that EGCG plays chemo-preventive roles in cancer prevention and treatment, especially in cases of colon, breast, stomach, esophagus, lung, and prostate cancers, melanoma, and head and neck carcinoma, including thyroid cancer.[69] The cumulative effect of two chemo-preventive polyphenols, curcumin (Cur) and EGCG, in achieving resistance against breast cancer was analyzed, and the results showed that EGCG effectively inhibited the growth and facilitated apoptosis in both doxorubicin (DOX)-sensitive and resistant MCF-7 cells, which were induced by Cur.[69] A research analysis that included 13 papers that conducted studies on populations spread across eight different countries recorded and represented data on the benefits of consumption of either green tea or black tea, or both, concerning the risk posed to breast cancer. The results of this meta-analysis indicated a lower risk for breast cancer associated with green tea consumption. However, the data suggested a possible late-stage, promotional effect of black tea on breast carcinogenesis.[70]

The anti-proliferative potency of various structurally dissimilar dietary flavonoids was compared in colon cancer cells, Caco-2 and HT-29, and in rat non-transformed intestinal crypt cells, IEC-6. The effect of the two most observed powerful dietary flavonoids used, quercetin and genistein, was seen to be dose-dependent. Their anti-proliferative potency varied significantly depending on structural differences, but the observations remained consistent with regard to the cells studied and were estimated to play an important role in cancer chemoprevention, especially in cases of the cancer of the gastrointestinal tract because of direct contact with food.[70]

Most of the cases of skin cancer reported worldwide are associated with non-melanoma (NMSC), caused chiefly due to chronic exposure to ultraviolet (UV) light and chemical carcinogens. UV light induces molecular signaling pathways such as Ras and MAP kinase, which result in specific genetic alterations that are crucial to the development of skin cancer. Cancer chemoprevention using oral dietary supplements or chemical intervention via the local application can lower the risk of cancer amongst high-risk populations. However, it is never definitive and universal. As a result, EGCG, a catechin derivative present in green tea that has antioxidant and sunscreen properties as well as the potential to inhibit UVB signal transduction activity, has been widely employed in chemoprevention to prevent the growth of skin cancers.[71] This research endeavor has also lured various cosmetic and pharmaceutical companies to boost their skin care products with green tea extracts in order to provide consumers with the appropriate amount of protection.[72]

Studies showed that green tea was capable of stimulating and increasing the anti-tumor activity of doxorubicin on Ehrlich ascites carcinoma tumors implanted in CDF1 and BDF1 mice. Green tea, in association with doxorubicin, increased the doxorubicin concentration in the tumors. However, the same effect of green tea was not recorded in normal, non-tumor cells. The enhanced inhibitory effects of doxorubicin induced by green tea on tumor growth were also noted in M5076 ovarian sarcoma, which is known to be less sensitive to doxorubicin. These studies suggested that the oral administration of green tea could encourage cancer chemotherapy and provide relief to cancer patients.[73]

**Antimicrobial Effect**

It has been reported that tea has significant antimicrobial activity against various pathogenic bacteria.[74] Earlier, the antimicrobial property of tea was reported by an army surgeon, who recommended the use of tea stored in bottles as a source of prophylactic against typhoid.[75] Regardless of the widespread consumption of tea in the world, there was a lacuna of proper evidence of antimicrobial property that was left unknown.

In the year 2005, R.P Tiwari *et al.* experimented with the synergistic antimicrobial effect of black and green tea. Both aqueous and organic solvent extracts were studied against Salmonella typhimurium 1402/84, S. Typhi Ty2a, Shigella dysenteriae, Yersinia enter ocolitica C770, and *Escherichia coli* (EPEC P2 1265), and found that black tea has got higher growth inhibitory concentration as compared to green tea. On the contrary, organic solvent green tea extract has shown better antimicrobial activity.[76]

In 2008, the anti-bacterial activities of the methanolic and aqueous extracts of *Camellia sinensis* on Listeria monocytogenes were investigated using agar gel diffusion, paper disc diffusion, and microdilution technique. Methanolic extraction of tea showed the highest anti-bacterial activity than the water extract.[77] Besides this, oolong tea also showed the highest anti-bacterial activity against Streptococcus mutants MT8148R; it was found to originate from monomeric polyphenol-rich fractions, which can readily bind to the protein, and this activity was stronger than that of pure polyphenols.[78]

Another antimicrobial activity was performed by Mehta *et al*. (2016), which prepared different concentrations of tea extracts and was assessed by the Agar Well Diffusion method. Both green and black tea were prepared in an aqueous, ethanolic, methanolic, and acetone medium. They have proved that in comparison with *E. coli* and P. *aeruginosa*, S. *aureus* (ATCC 25922) has been found to be more susceptible to aqueous tea extracts.[74]

It has been studied that the antimicrobial activity decreased with the increase in the extent of tea fermentation during processing. Green tea, which is not fermented, exerts the most potent antimicrobial activity, followed by the partial or semi-fermented beverage. Black tea, which is entirely fermented, showed the least antimicrobial activity. It was also seen that the microbial properties of tea depend upon the manufacturing seasons of tea. The extracts of oolong tea prepared in summer showed the highest antimicrobial activity in comparison with other flushes of tea made in spring, winter, and fall.[79] Taylerson (2012) concluded that catechins from non-fermented varieties of *Camellia sinensis* show antimicrobial activities that can provide potential protection from cancers, cardiovascular diseases, and dental caries. However, black tea, which is known to be completely oxidized and whose catechins have been converted to thearubigins and theaflavins, shows lesser antimicrobial activity in comparison.[80] Studies showed that (−)−EGCG, one of the main constituents of tea polyphenols, inhibited the development and growth of bacterial spores in Bacillus *stearothermophilus* – a thermophilic spore-forming bacterium and *Clostridium thermoaceticum*, an anaerobic spore – forming bacterium.[81] In a different study by Sakanaka *et al.* (1989), it was shown that Japanese green tea extracts could inhibit the growth of *Streptococcus mutans*, which is a causal organism of dental carries. This inhibitory property can be attributed to polyphenolic compounds, mainly GC, EGC, and EGCG.

The commonly consumed beverage, tea, thus has multi-dimensional effects such as antimicrobial activity, inhibitory action on the bacterial and salivary amylase, and inhibition of production of acid.[82] It was seen that green tea and black tea extracts, along with two of their main bioactive compounds, EGCG and theaflavins, may be of interest for the treatment of Fuso bacteriumnucleatum-associated disorders, as they prevented biofilm formation by the bacteria, decreased its adherence to oral epithelial cells and matrix proteins and displayed anti-bacterial activity that might involve damage to the bacterial cell membrane of *F. nucleatum*, which is an oral bacterium indigenous to the human oral cavity, playing a significant role in periodontal disease.[83] Bacterial infections in fish are one of the most leading causes of fish mortality and might cause a significant economic crisis on a global scale. Green tea seed (watered tea seed [WTS]) powder and its secondary metabolite saponin used as feed additives showed significant antimicrobial activity and potential disease prevention capability in the bacterial fish pathogen, *Listonellaanguillarum*, that infect rainbow trout (*Oncorhynchus mykiss*, Walbaum).[84]

It has been seen that gold and silver nanoparticles prepared from the extracts of green and black varieties of leaves of *Camellia sinensis*, when immobilized on cotton clothes, displayed high anti-bacterial activity and the characteristic color, thus indicating potential use as antimicrobial pigments.[85] Silver nanoparticles prepared by green synthesis using green tea extracts showed anti-bacterial

activity for the bacterial strains – *Staphylococcus aureus* and *Escherichia coli*.[86]

Theaflavins and their derivatives are the unique bioactive components and are collectively called theaflavins (TFs). TFs are found in black tea that is produced as a result of the fermentation of green tea leaves. They are mainly responsible for the antioxidant activity of black tea. In addition to being key antioxidant bioactive components, TFs and flavonoids are also non-cytotoxic to normal human cells and are, hence, employed in several therapeutic applications. A recent study showed that TFs and flavonoids' rich extract stabilized silver nanoparticles acted as better anti-bacterial agents.[87] The above-mentioned studies represented that the antimicrobial potential of the tea and its bioactive ingredients.

**Tea and Toxicology**

Tea has known to provide many potential benefits to our health. *Camellia sinensis* has shown surprising activity; it is anti-diabetic,[49] anti-cancer,[88] anti-bacterial,[89] neuro-protective,[90] cardio-protective,[91] anti-obesity,[92] hepato-protective,[93] and anti-viral.[89] However, besides possessing the good qualities, very few studies have shown that tea has some toxic effect under certain conditions. Among the different varieties of tea, the green tea has some side effects when consumed in high amount, while for the black, oolong and white teas, no such evidence is recorded.

**Tea Infusion Procedure and Their Impact on Liquor Characteristics**

Tea is a refreshing drink with unique taste and aroma. Tea is the world's second most popular beverage after water.[94] Almost two-thirds of the world's population consumes it at least once a day regularly.[95] Tea preparation and brewing procedures vary considerably around the world.[96] For different types of teas, the conventional method is to steep the tea leaves in boiling water for 1 to 10 minutes at 70–100°C.[97] Darjeeling black tea is customarily brewed by steeping the leaves for five minutes in hot water (90–100°C). Then it is either consumed as liquor or consumed with milk and sugar.[97] The addition of milk can have two different effects on the antioxidant content of tea. Milk reduced the ABTS+ radical scavenging capacity (an electron transfer-based assay) of Darjeeling (8.3%), green (6.0%) and English breakfast (19.6%) teas in one hand. On the other hand, milk increased the chain-breaking antioxidant capacity of teas in the lipid peroxidation technique by 19%, 12% and 10% for green tea, English breakfast tea and Darjeeling tea, respectively.[98]

Cold tea infusion, as opposed to hot tea, is a revolutionary way of brewing tea that has recently acquired popularity in China, particularly during the summer months.[99,100] The consumption patterns of Taiwanese consumers for new and different forms of cold infusion tea products have also diverged from those for classic hot infusion ones.[101] However, only a few people knew the cold brew procedure and its expanding market.[102]

Because hot tea has little health risks, no one considered it should be substituted with cold tea. As science and technology advance, people become increasingly aware of the detrimental effects of drinking too much hot tea. It was found that consuming very hot tea (>65°C) was substantially related to a higher risk of oesophageal squamous cell cancer compared to non-drinkers.[103,104]

There are around 4,000 different types of bioactive compounds found in tea, with polyphenols making up 33 percent of the total and catechins being the most frequent. There are many different types of chemical components, including alkaloids, amino acids, carbohydrates, proteins, chlorophyll, volatile organic compounds, and trace elements.[105] The conditions under which green tea is brewed can have a variety of effects on the metabolic and catechin profiles, as well as the antioxidant capacity of the resulting infusions.[106] Therefore the relative concentrations of those bioactive constituents in tea brew can be correlated with the human health promoting activities and thereafter enhancing their curative nature towards different health problems.[107] It was found that some bioactive substances, such as tannin and caffeine, can have both beneficial and adverse effects on the body's health when eaten in significant quantities with tea brew or tea infusion. Solubility of caffeine (http://www.sciencemadness.org/smwiki/index.php/Caffeine/) and tannin are higher in hot water than cold. It was also found that cold infusion of white tea provided higher phenols, catechins and flavonoids than hot water infusion of white tea and cold tea infusions had much higher

antioxidant activity than hot tea.[108,109] However, cold brewing with a lower extraction efficacy resulted in lighter, less pigmented and higher sensory-rated tea infusions, with a less astringent and bitter flavour. Another research showed that cold brewing reduces the concentration of numerous components, including soluble solids, caffeine, and antioxidants. Cold brewing is less efficient Cold brewing yielded clearer, less-colored, and higher-scoring tea infusions. Cold-brewed tea infusions had lower caffeine, EGCG, and EGC contents and a softer flavour.[110] The chemical components of cold tea infusions increased with brewing duration, with the highest increase occurring within the first two hours of brewing.[111] All chemical components tested, except for caffeine, were higher in cold tea infusions over eight hours than in hot tea infusions. In addition, cold tea infusion antioxidant capacity rose with brewing time and reached a plateau after 12 hours.[112,113] The above facts may attract tea lovers towards cold tea brew.

**Conclusion**

Natural substances have endless potential in the pharmaceutical sector, not only for managing specific diseases but also for increasing natural immunity. In such a setting, tea, as a medicinal plant, can play a magnanimous role due to its relative ease of availability and simple acceptance among the masses as a part of a big population's daily living habit. Tea's full potential must be realised by massive efforts. During the brewing process, many phytochemicals are lost due to poor extraction from the tea leaves or thermo-labile phytochemical degradation. Tea is expensive due of its growth and processing. Research and development on quantitatively optimising the tea brewing process is urgently needed to take tea's benefits either through conventional household brewing or processed beverage, whose market is developing rapidly. In a post-pandemic world, the goal is to make tea's health advantages accessible to all; hence creative ways that enhance tea polyphenol absorption and bioavailability should be explored.

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**Conflict of Interest**

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